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Investigating The Effect Of Individual-Level And Neighborhood-Level Exposures On Delivery Outcomes

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Abstract

Globally, rates of maternal morbidity and mortality have declined; however, in the United States they continue to climb. In this dissertation we investigated individual-level and neighborhood-level exposures and their roles on adverse delivery outcomes, including severe maternal morbidity and cesarean delivery after labor induction. First, we developed a novel algorithm for large Electronic Health Record datasets to determine whether a patient has experienced residential mobility, (i.e., moved to another residence), during pregnancy, or any other time period of interest. The goal of this algorithm is to construct low-cost patient residential histories so as to more accurately assign geo-spatial exposures, such as poverty or violent crime, in epidemiologic studies. By taking residential mobility into consideration, the level of exposure misclassification is mitigated. Secondly, we investigated severe maternal morbidity in the University of Pennsylvania Health System, assessing the role of individual-level and neighborhood-level exposures in these life-changing outcomes. We demonstrated that the persistent racial disparities seen in national rates of severe maternal morbidity exist among our health system as well. Indeed, race at the individual-level, and proportion of people identifying as Black per census tract at the neighborhood-level, were associated with increased risk of severe maternal morbidity. Thirdly, we explored the effect of neighborhood deprivation on post-induction cesarean deliveries. Labor inductions are common, in fact 20% of pregnant people will experience a labor induction during delivery. Among those over one-third will have a post-induction cesarean delivery. Importantly, a disproportionately high number of people experiencing a post-induction cesarean delivery are people of color. Neighborhood deprivation has been shown to be associated with adverse health outcomes such as cancer, and adverse pregnancy outcomes such as preterm birth. We evaluated the link between neighborhood deprivation and cesarean delivery among women undergoing labor induction, an area of limited prior study. We found that neighborhood deprivation increases the risk of post-induction cesarean delivery, even after adjusting for important individual-level covariates, such as pregnancy-related hypertension. This dissertation study demonstrates the importance of individual-level and neighborhood-level context in understanding the increasing trends of adverse delivery outcomes, and for shedding light on underlying factors involved in racial health disparities.

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INVESTIGATING THE EFFECT OF INDIVIDUAL-LEVEL AND NEIGHBORHOOD-LEVEL EXPOSURES ON DELIVERY OUTCOMES

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INVESTIGATING THE EFFECT OF INDIVIDUAL-LEVEL AND NEIGHBORHOOD-LEVEL EXPOSURES ON DELIVERY OUTCOMES

DEDICATION PAGE

For Kayleigh and Callahan. You would not be here today if not for the maternal health clinicians and researchers who have come before me. I am honored to make my own contribution in your names.

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ABSTRACT

INVESTIGATING THE EFFECT OF INDIVIDUAL-LEVEL AND NEIGHBORHOOD-LEVEL EXPOSURES ON DELIVERY OUTCOMES

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Globally, rates of maternal morbidity and mortality have declined; however, in the United States they continue to climb. In this dissertation we investigated individual-level and neighborhood-level exposures and their roles on adverse delivery outcomes, including severe maternal morbidity and cesarean delivery after labor induction. First, we developed a novel algorithm for large Electronic Health Record datasets to determine whether a patient has experienced residential mobility, (i.e., moved to another residence), during pregnancy, or any other time period of interest. The goal of this algorithm is to construct low-cost patient residential histories so as to more accurately assign geo-spatial exposures, such as poverty or violent crime, in epidemiologic studies. By taking residential mobility into consideration, the level of exposure misclassification is mitigated. Secondly, we investigated severe maternal morbidity in the University of Pennsylvania Health System, assessing the role of individual-level and neighborhood-level exposures in these life-changing outcomes. We demonstrated that the persistent racial disparities seen in national rates of severe maternal morbidity exist among our health system as well. Indeed, race at the individual-level, and proportion of people identifying as Black per census tract at the neighborhood-level, were associated with increased risk of severe maternal morbidity. Thirdly, we explored the effect of neighborhood deprivation on post-induction cesarean deliveries. Labor inductions are common, in fact 20% of pregnant people will experience a labor induction during delivery. Among those over one-third will have a post-induction cesarean delivery. Importantly, a disproportionately high number of people experiencing a post-induction cesarean delivery are people of color. Neighborhood deprivation has been shown to be associated with adverse health outcomes such as cancer, and adverse pregnancy outcomes such as preterm birth. We

evaluated the link between neighborhood deprivation and cesarean delivery among women undergoing labor induction, an area of limited prior study. We found that neighborhood deprivation increases the risk of post-induction cesarean delivery, even after adjusting for important individual-level covariates, such as pregnancy-related hypertension. This dissertation study demonstrates the importance of individual-level and neighborhood-level context in understanding the increasing trends of adverse delivery outcomes, and for shedding light on underlying factors involved in racial health disparities.

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CHAPTER 1: INTRODUCTION

1.1 Maternal Morbidity and Mortality

Maternal morbidity and mortality persist as key indicators of women's health both globally and in the United States (US). However, while maternal mortality rates have been declining globally, they have continued to increase in the US (Collaborators, 2016). In fact, pregnancy-related deaths in the US have doubled between 1987 and 2014 from 7.2 to 18.0 deaths per 100,000 live births (Prevention). While mortality continues to increase in the US, severe maternal morbidity is 100 times more common in the US than maternal mortality (Creanga, 2017; A. A. Creanga et al., 2014). Severe maternal morbidity includes unexpected, poor outcomes of labor or delivery that may result in short or long term consequences that are significant for the women and their family (Prevention). The World Health Organization (WHO) has brought into focus the need for research into these stark rates of poor maternal health outcomes in the US The optimal, life-saving rate of cesarean deliveries is debated somewhat in the literature, however the WHO has indicated that the optimal rate should be between 10-15% (Chalmers, 1992), beyond that threshold maternal and neonatal mortality rates do not decline any further. However, the rate of cesarean delivery in the United States has steadily increased to rates well above 30%, resulting in many negative downstream health effects. Some research suggests that increased rates of cesarean deliveries are associated with poor neonatal and maternal outcomes, such as increased risk of severe maternal morbidity and neonatal intensive care admissions (Gibbons et al., 2010; Lumbiganon et al., 2010). For the purposes of this dissertation, we focus on the adverse maternal health outcomes of delivery, while remaining cognizant that adverse maternal health outcomes affect neonatal outcomes as well. The purpose of this dissertation is to understand the individual and neighborhood-level risk factors that alter a women's risk of severe maternal morbidity and cesarean delivery following induction (colloquially a 'failed induction'). To achieve this end, we develop an informatics method to address residential mobility in longitudinal geo-spatial exposure studies (chapter 2), we investigate individual-level and neighborhood-level risk factors of severe maternal morbidity (chapter 3), and we explore the relationship between neighborhood deprivation and cesarean delivery after induction (chapter 4).

1.2 Motivation

The remarkable rates of maternal morbidity and mortality in this country have been the main motivation of this dissertation work. However, it is of great importance to note that these rates do not affect the US population uniformly. It is known that major racial disparities exist among maternal morbidity, maternal mortality, and rates of cesarean delivery that cannot be explained by genetics (Cabral, Fried, Levenson, Amaro, & Zuckerman, 1990; David & Collins, 1997). It is for this reason that we found it imperative to create a method that would allow research on delivery outcomes to be more accurate, and to investigate the rates of severe maternal morbidity and cesarean deliveries after induction.

Significant racial and ethnic disparities persist for both severe maternal morbidity and maternal mortality. Indeed, studies show that the risk of severe maternal morbidity and mortality is markedly increased among people of color (H. H. Burris et al., 2019; Collaborators, 2016; N. Krieger, Williams, & Moss, 1997). Black American women are upwards of four times as likely to die of complications from pregnancy as compared to White women (Collaborators, 2016; Creanga, 2017; A. A. Creanga et al., 2014) and they have a ten-fold increased risk of experiencing severe maternal morbidity (Fingar, Hambrick, Heslin, & Moore, 2018). Medical comorbidities, maternal education or income, do not explain the observed disparity in severe maternal morbidity. Krieger *et al.* have shown structural racism and historical segregation of neighborhoods to be drivers of adverse health outcomes (Bailey et al., 2017; Nancy Krieger et al., 2020). As such, it is important to better understand the role of neighborhood context itself as a disparity in maternal morbidity outcomes.

The American College of Obstetrics and Gynecology has noted major concern over the rapid increase of cesarean deliveries over the last couple of decades (Caughey et al., 2014). More than

20% of delivering people will undergo a labor induction, and one-third of them will have a cesarean delivery (*National Vital Statistics Reports, Births: Final Data for 2018*, 2019; "Recent declines in induction of labor by gestational age," 2016; *WHO recommendations for induction of labour*, 2011). Among the rates of unnecessarily high cesarean deliveries, there have been large racial disparities in delivery outcomes in the US (Hirshberg & Srinivas, 2017; Obstetricians & Gynecologists, 2015). Specifically, Black Americans are more likely than White patients to undergo a cesarean delivery, even when adjusting for both sociodemographic and clinical differences (Yee et al., 2017). While the cause of racial disparities in health is complicated, racial disparities persist even when interventions are integrated to address implicit clinical biases (Hamm, Srinivas, & Levine, 2020). Longstanding racial residential segregation leads to large differences in neighborhood environmental exposures by race in the United States (Heather H Burris & Hacker, 2017; Mehra, Boyd, & Ickovics, 2017). Indeed a recent paper by Nardone *et al.* illustrates the deleterious effect of redlining on birth outcomes (Nardone et al., 2020). Given the known interaction of environmental stressors on hormonal pathways (Harris & Seckl, 2011; Henson & Chedrese, 2004; Mehra et al., 2017; Patisaul & Adewale, 2009; Whirledge & Cidlowski, 2010), it is biologically plausible that patients from different neighborhood contexts and exposure profiles may respond more or less favorably to labor induction (Table 1.1)

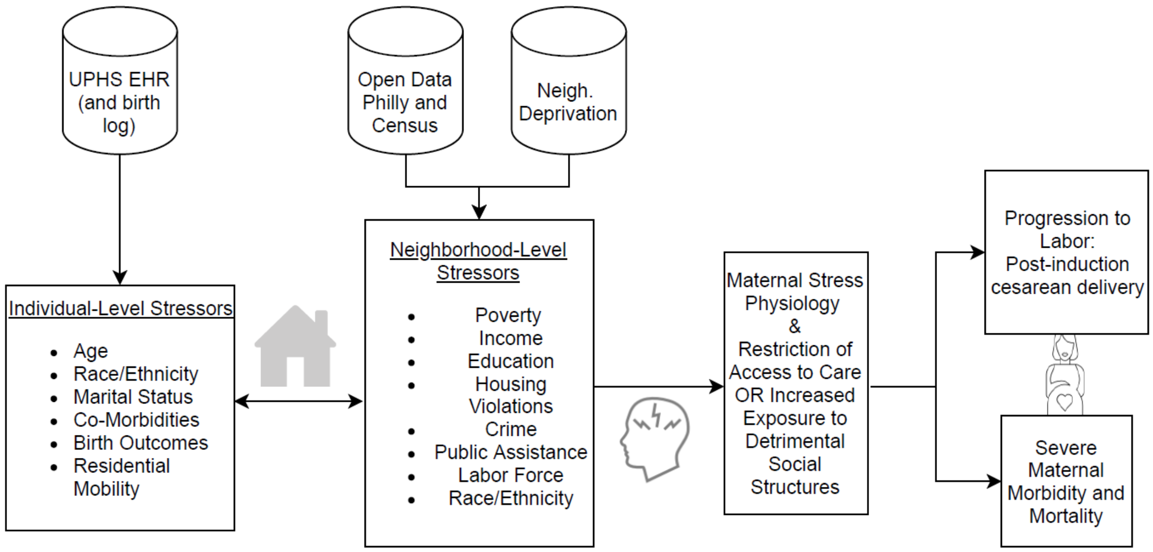

Figure 1.1: Dissertation study conceptual model illustrating the plausibility of the effect of individual-level and neighborhood-level stressors on post-induction cesarean delivery and severe maternal morbidity.

1.3 Epidemiological background and developments

In the second chapter we propose a novel method to identify residential mobility from address information recorded in the Electronic Health Record (EHR) in the context of longitudinal geo-spatial exposures studies, which infer environmental, social, and economic exposures from address information from the error-riddled EHR. This challenge of the EHR makes it difficult to determine if a patient has moved, which is integral for achieving accurate exposure assessment. As such our goal was to create an algorithm to identify residential mobility during pregnancy in a cohort of pregnant patients from Penn Medicine with address information from the EHR.

Epidemiologic studies often use an individual's residential address to assign a proxy measure of neighborhood-level exposures including exposure to natural environmental toxicants (Daly et al., 2018), green space (Hystad et al., 2014), poverty and violent crime (Signorello et al., 2014). Researcher's often choose to assign these exposures based on an individual's most current address; however, that assumes that a person is not mobile at the time of outcome event, or during the study enrollment, or relevant period of exposure (D. C. Wheeler & Wang, 2015).

Indeed, the population of the United States is known for being highly mobile, which has been shown to cause misclassification of environmental exposures for outcomes with long latency periods (Manjourides & Pagano, 2011; D. Wheeler & Calder, 2016). As such, it is important to consider a person's residential history.

Our work builds on other studies, which have found accounting for residential mobility to be important to avoiding differential exposure misclassification (Brokamp, LeMasters, & Ryan, 2016; Pennington et al., 2017; D. C. Wheeler & Wang, 2015). Other studies have constructed residential histories in small, carefully followed prospective cohorts, or by using Lexus Nexus (an expensive third-party software). There has not been an open-source freely available algorithm that could be used in large retrospective cohort studies to identify residential mobility from the EHR. The challenge of EHR data is that the address information is often entered inaccurately and hastily resulting in the need for address disambiguation. Therefore, we create an algorithm entitled REMAP (a Relocation Event Moving Algorithm for Patients), which is very accurate (>95%) at classifying residential mobility. This tool can be used to lower the rate of geo-spatial exposure misclassification.

In the third chapter we investigate the association between individual-level and neighborhood-level risk factors and the effect on risk of severe maternal morbidity. National severe maternal morbidity rates have been calculated and reported by the Centers of Disease Control and Prevention (CDC) since 1993, with the most recent report being released in 2014. Using administrative hospital discharge data and International Classification of Diseases procedure and diagnosis codes, the CDC has compiled a list of 21 indicators of severe maternal morbidity, which is what we used as our outcome measure in this chapter. Per the CDC's reports, severe maternal morbidity has risen by 75% in the last decade in the US, affecting more than 52,000 women annually (Callaghan, Creanga, & Kuklina, 2012). Black Americans are four times more likely to die of pregnancy complications and ten times more likely to experience one of the indicators of severe maternal morbidity as compared to White Americans (Collaborators, 2016; Creanga, 2017; A. A. Creanga et al., 2014; Fingar et al., 2018).

Often studies interrogating racial disparities in severe maternal morbidity outcomes focus on individual-level characteristics such as maternal education or income, or medical comorbidities; however, these factors alone do not explain the persistent disparity among outcomes. The role of social determinants of health in severe maternal morbidity has historically been an understudied area of maternal morbidity research. Critical work done by Krieger *et al.* in the structural racism space has illustrated the role of historical segregation of neighborhoods in driving poor birth outcomes (Bailey et al., 2017; Nancy Krieger et al., 2020). In this chapter we build off the work of Krieger *et al.* and others to better understand the role of neighborhood disparities and racism in severe maternal morbidity. Specifically, we add to the body of severe maternal morbidity research by exploring the individual-level and neighborhood-level risk factors of severe maternal morbidity.

In the fourth chapter we interrogate the association of neighborhood deprivation and individual-level characteristics with cesarean delivery following a labor induction. In this chapter we utilize the University of Wisconsin's Neighborhood Atlas Area Deprivation Index, composed of 17 measures encompassing education, employment, housing-quality and poverty, derived from the Census American Community Survey and long-form data. We used a generalized linear mixed model to model neighborhood deprivation in two ways, in categorical levels: "highest", "high", "moderate", and "lowest" levels of neighborhood deprivation, and as a non-linear spline. By binning the exposure into levels of deprivation we hoped to provide a more interpretable clinical measure of the association between neighborhood deprivation and cesarean delivery after labor induction.

More than 20% of patients who deliver in the United States undergo labor induction, and more than a third of these patients will have a cesarean delivery, which is associated with several morbidities. As such, a successful labor induction to delivering patients is often seen as one that ends in a vaginal delivery. While some research has been done to predict cesarean delivery after induction, limited studies have considered any measures of neighborhood-level deprivation. Thus, in this chapter we add to the body of literature by evaluating neighborhood-level context to the clinical, individual-level focused work that has been completed thus far. Lastly, in the fifth chapter, we discuss our conclusions and further directions for study.

CHAPTER 2: AN ALGORITHM TO IDENTIFY RESIDENTIAL MOBILITY FROM ELECTRONIC HEALTH RECORD DATA

2.1. Background

2.1.1. Longitudinal epidemiologic studies often assign environmental exposure estimates based on residential address.

Epidemiologic studies often utilize an individual's residential address to assign estimates of neighborhood-level environmental exposures. Geo-spatial factors to which someone might be exposed on a daily basis include toxicants in the natural environment, such as drinking water contaminants (Daly et al., 2018), air pollution (Mirabelli, Vaidyanathan, Flanders, Qin, & Garbe, 2016), variables characterizing the built environment including walkability (Frank et al., 2006), park access, and green space (Hystad et al., 2014), and socioeconomic characteristics such as neighborhood income, food access (Shannon, 2016), and violent crime (Signorello et al., 2014). The study of these environmental variables is common in longitudinal studies, especially in health disparities research and even clinical studies (Padilla, Kihal-Talantikit, Perez, & Deguen, 2016; Palumbo, Wiebe, Kassam-Adams, & Richmond, 2019). Thus, it is critical for local, state and federal budgetary considerations and dispersal of resources, to accurately characterize these exposures in epidemiology association studies.

2.1.2. Epidemiologic studies often do not consider residential mobility, which could lead to misclassification of the exposure.

Accurate information regarding residential address is crucial, especially as geo-spatial techniques to study environmental exposures with health outcomes become more common in public health research (Blanchard, Deguen, Kihal-Talantikite, Francois, & Zmirou-Navier, 2018; Xie, Greenblatt, Levy, & Himes, 2017; Xie & Himes, 2018). As such, residential mobility is a vitally important consideration in longitudinal studies. However, studies often do not consider mobility of subjects across time (Blanchard et al., 2018; Fell, Dodds, & King, 2004; Hodgson, Lurz, Shirley, Bythell, & Rankin, 2015; Pennington et al., 2017). Rather, most investigators focus on location as a static point without incorporating residential mobility, or moves (Boscoe, 2011; Brauer et al., 2007; Gehring et al., 2010). The assumption is that the most current address is the relevant time of exposure and that the patient is not mobile over time. However, as stated by Wheeler and Wang, the incorrect assumption being made is that the population is not mobile and thus time of event or study enrollment is the relevant period of exposure (D. C. Wheeler & Wang, 2015). However, it is known that population mobility in the US is high enough to distort the spatial signal of environmental exposures for diseases or outcomes with long latency periods (Manjourides & Pagano, 2011; D. Wheeler & Calder, 2016). Residential mobility is important to incorporate into exposure assessment to avoid differential misclassification, which can bias results either towards, or away from the null hypothesis (Brokamp et al., 2016; Pennington et al., 2017; D. C. Wheeler & Wang, 2015). Studies looking into residential mobility have been contradictory. In a study of changes in residential proximity to road traffic and the risk of death from coronary heart disease, Gan et al. found that accounting for residential mobility strengthened the association (Gan et al., 2010). In contrast, Canfield et al. found associations to be small and differential when accounting for residential mobility in a study of residential mobility patterns and the association with birth defects (Canfield, Ramadhani, Langlois, & Waller, 2006).

2.1.3. Assigning partial exposures accurately is critical, especially in heterogeneous areas.

The inconclusive nature of these prior studies points to the necessity of being able to determine whether a subject moved, so as to accurately assign partial exposures accurately. This is particularly important in heterogeneous areas, such as urban areas, where the environment can differ across neighborhoods. People relocate, and it is especially important to capture this information during longitudinal studies. Fundamentally, longitudinal studies are utilized to investigate vulnerable time periods – some length of time preceding an outcome of interest during which participants might be most susceptible to an exposure, which is inherently important to consider for long outcome latency (Dadvand et al., 2013; Guxens et al., 2014; D. C. Wheeler &

Wang, 2015). Pregnancy, in particular, is a dynamic period when exposures during a specific trimester might be more important than another and it is important to capture that information. Therefore, assuming a constant exposure across all trimesters throughout a study period may lead to biases. Additionally, as residential mobility is likely associated with covariates such as poverty, not accounting for mobility could result in differential misclassification (Brokamp et al., 2016).

2.1.4. Informatics methods are needed to solve this problem.

To our knowledge no study has put forth an algorithm that can deal with very large Electronic Health Records (EHRs) that contain both administrative errors and true relocation events. Some studies have worked to address the problem of relocation events in recruited cohorts using LexisNexis; however, these data are inherently different and easier to work with than large, error-riddled, EHR data (Fecht et al., 2020; D. C. Wheeler & Wang, 2015). Although LexisNexis provides cleaner address data than the EHR, it is not free to access or use. Furthermore, Wheeler and Wang found that the enhanced, more expensive LexisNexis service was more accurate than the basic service (D. C. Wheeler & Wang, 2015). Given that the subscription cost of LexisNexis makes it inaccessible to many researchers, and that the accuracy of LexisNexis residential histories have shown to be of variable accuracy, use of accessible and up-to-date EHR address information is preferable (Jacquez et al., 2011).

Many exposure studies that investigate pregnancy or delivery outcomes, assign exposure based upon address at time of delivery or an address during the first or last trimester, which may be the most vulnerable times in a pregnancy (Ritz, Wilhelm, Hoggatt, & Ghosh, 2007; Smith et al., 2017). However, we assert that pregnant patients move during their pregnancies and that it is important to capture these relocation events so as to accurately examine environmental exposure estimates. The aim of this study is to develop an algorithm that utilizes address information from the EHR to automatically determine if a patient has moved so as to enable assignment of partial, time-specific neighborhood-level exposures. We hypothesize that by identifying, and accounting for, these residential mobility events, exposure misclassification can be avoided.

2.2. Methods

2.2.1. Data source

For this study, we used pregnant patients in the University of Pennsylvania Health System (UPHS) also called Penn Medicine. The dataset includes information from the Electronic Health Record (EHR) from every visit within one year prior to delivery and includes a field for current address at time of each visit, as illustrated in **Figure 2.1**. For the purpose of the development of this algorithm, we chose to focus on a study population of pregnant patients derived from department-managed delivery logs (**Figure 2.2**).

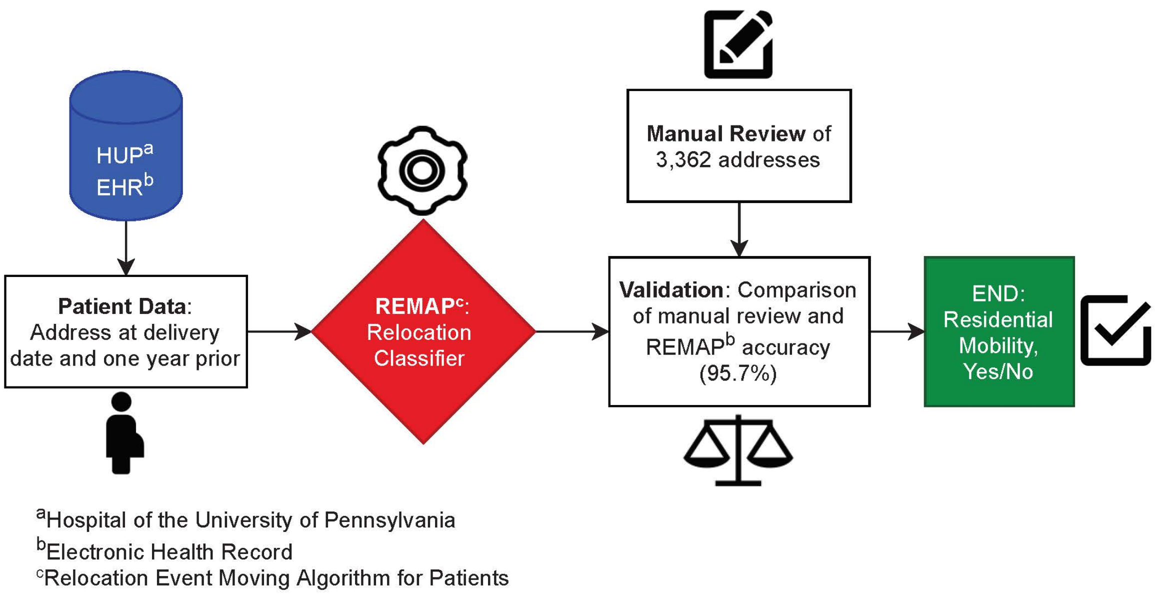

Figure 2.1: Overview of REMAP development and validation process.

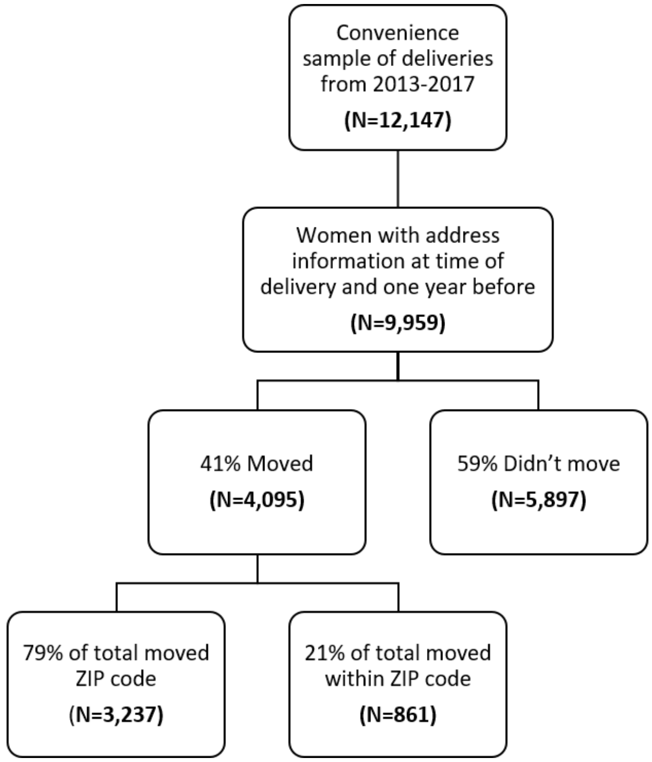

Figure 2.2. Flowchart Showing Our Cohort and Breakdown by Moving Status. Note: there were 3 patients who moved both within zip code and across zip codes within one year before they delivered.

2.2.2. Data cleaning

Every encounter that a patient had with the health system had a corresponding address field completed. Therefore, we had a patient-reported, current address for every visit for one year prior to delivery. **Figure 2.3** shows in detail how REMAP functions to determine residential mobility. Our first step was to clean the address data of administrative errors, so as to be able to compare two addresses successfully to determine whether a move had occurred (**Figure 2.1 and Figure 2.3**). First, we made all text uppercase, as some addresses where all uppercase, some were all lowercase, and others were a heterogeneous mix of both cases. Secondly, we abbreviated street and avenue, as often these designations were abbreviated in the EHR. Thirdly, we discarded all unit and apartment number information (**Figure 2.3 and Figure A.1)**. This choice was made because in many cases it was absent for one address entry.

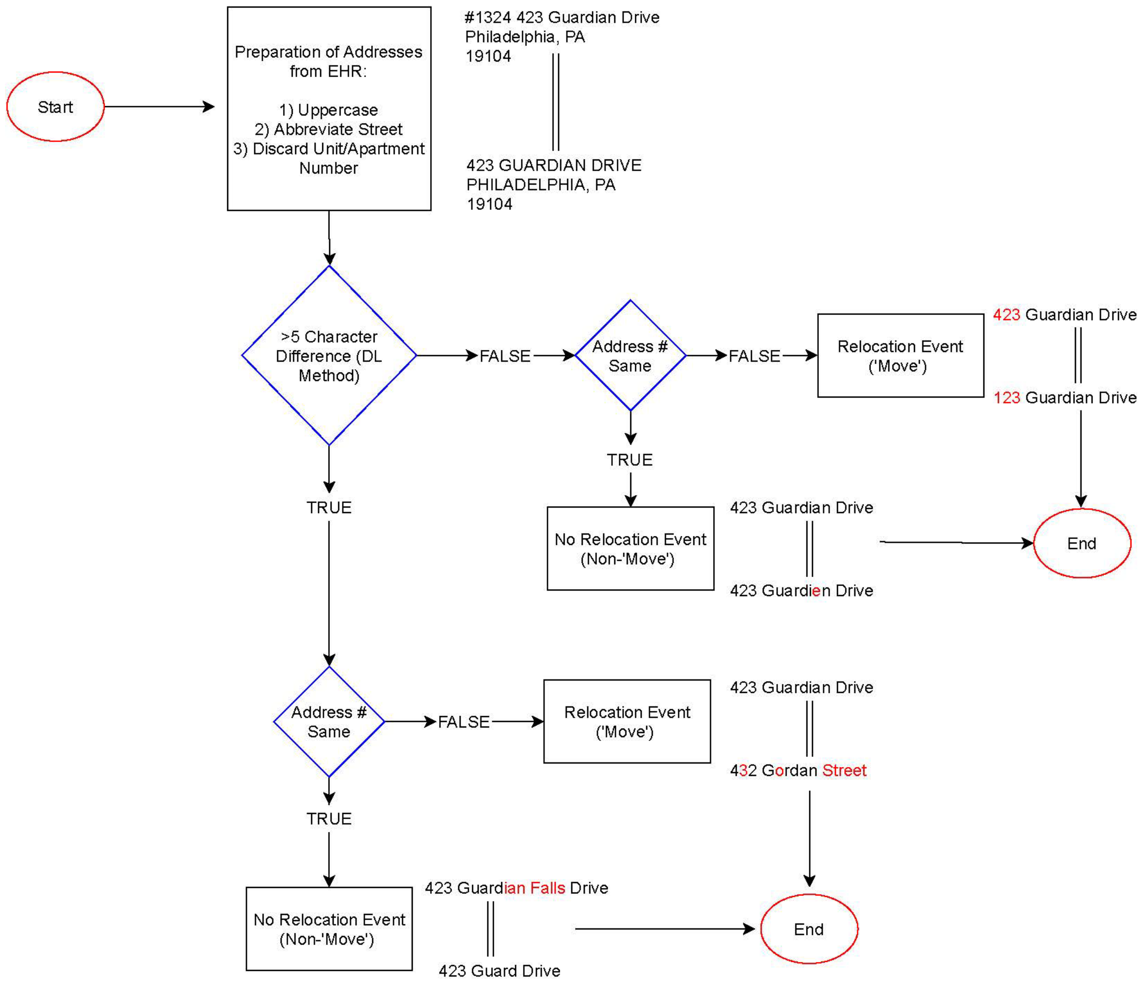

Figure 2.3: Algorithm for identifying residential mobility from Electronic Health Records.

2.2.3. REMAP: rule generation

After cleaning the data, we created relocation classifying rules for our relocation algorithm (**Figure 2.1** and **Figure 2.3**). To determine whether a patient had moved, our goal was to determine whether the address at delivery was the same or different from the address one year prior. To do so we needed to decide what functional differences between addresses would be informative in classifying the comparison as a move or not. We used the Damerau–Levenshtein

(DL) distance string metric to determine the number of character differences between addresses (Bard, 2006). The DL metric was chosen because it allows for transpositions, for example “Guardian” and “Gaurdian” would be recognized as being the same street name (**Figure 2.3 and Figure A.1**). To begin, we chose to set our threshold of character differences as being five. If there were five or fewer character differences, the classifier system would initially say that there was not a move. If there were more than five-character differences, it would determine that there had been a move. Next, to tune the algorithm, we included the rule that if a first numeric variable was present, and if it was the same as the other record’s numeric variable, then it would be counted as a non-move (e.g., "423 Guardian Drive" and "423 Guard Dr" would be considered a non-move even though there are 6 changes between the 2 addresses). Conversely, we determined that even if the character difference were less than or equal to five, but the address number was present and different (“423 Guardian Drive” and “123 Guardian Drive”) it would be counted as a move (**Figure 2.1** and **Figure 2.3**).

2.2.4. Validation of REMAP

To validate REMAP we manually reviewed 3,362 addresses to determine the accuracy of the algorithm (**Figure 2.1**). We also calculated the sensitivity, specificity, and the F1 value for the REMAP algorithm. Furthermore, we compared REMAP to a simpler technique of comparing the ZIP code at time of delivery and one year prior to delivery to see if the comparison of ZIP code alone could accurately determine residential mobility. REMAP compares the addresses in their entirety and has a number of tuning rules built in, and is thus more complex.

2.2.5. Importance of REMAP: area deprivation

To determine whether misclassification would occur when using a real-world example, we utilized the Area Deprivation Index (ADI), composed of 17 education, employment, housing-quality and poverty measures from long-form Census data and American Community Survey (ACS) data (Kind & Buckingham, 2018). We assigned the area deprivation score to each person in the cohort both taking residential mobility into account, looking at address at delivery and one year prior, and not taking it into account, only looking at address at delivery. We then assessed what the percentage of misclassification was when not taking mobility into account by looking at the percentage of area deprivation scores that changed in the overall cohort. We then created a threshold for misclassification of about one standard deviation difference in deprivation score (SD = 27) (**Figure 2.4**). Indeed, many studies that utilize the ADI as an exposure choose to bin the continuous exposure into groupings of percentiles, or most and least disadvantaged (Durfey, Kind, Buckingham, DuGoff, & Trivedi, 2019; Hu, Kind, & Nerenz, 2018). For each pregnancy, we binned the change in deprivation score into quartiles. In addition, evidence of differential misclassification was assessed by comparing a map of the block level Area Deprivation Index in Philadelphia and a map of the percent of patients who moved in pregnancy per tract they lived in at delivery. We examined whether patients moved to areas of higher or lower deprivation during pregnancy (**Figure 2.5**). We used R version 3.6.1 for all analysis. The University of Pennsylvania's Institutional Review Board approved this study.

2.3. Results

2.3.1 Study population

Our study population was derived from a convenience sample of 12,147 deliveries from the departmental delivery logs at the Hospital of the University of Pennsylvania from 2013-2017. Of those 12,147 deliveries we had address information at both time of delivery and one year prior for 9,959 patients (**Figure 2.4**). Of these 9,959 patients, 41% moved and 59% didn’t move. Among those who did move, 79% changed zip code and 21% moved within their ZIP code (**Figure 2.2**). We geocoded the addresses both at time of delivery and one year prior using ArcGIS. This resulted in a dataset of 8,384 patients with correctly geocoded addresses both at time of delivery and one year prior.

2.3.2. Accuracy of the residential mobility algorithm

To validate our algorithm and assess its accuracy, we manually reviewed 3,362 addresses to determine whether a patient had moved or not (**Figure 2.1**). This gold standard determination was then compared against the classifications made by our algorithm. We found that REMAP was 95.7% accurate (95% CI 94.7%-96.7%), with a sensitivity of 97.1% (95% CI 96.2%-98.0%), a PPV of 93.8% (95% CI 92.7%-95.0%), and a specificity of 94.5% (95% CI 93%-96%). Our algorithm outperformed us using only changes in ZIP codes to determine residential mobility when we compared this method during our period of manual review. A change in ZIP code from the address at delivery compared to the address at one year prior achieved only 82.9% accuracy in determining residential mobility, during our manual review process. The reason comparing ZIP codes to determine residential mobility was sub-par to REMAP was: a) moves occurred within ZIP code and b) data entry errors with the ZIP codes (e.g., inversion of numbers). REMAP performed much better because it was robust enough to identify moves within ZIP codes and was not as dependent on inversions.

2.3.3. Misclassification in area deprivation score

When not taking residential mobility into account when assigning area deprivation scores to each patient, the exposure of deprivation was misclassified 39% of the time when examining any change in deprivation. When looking at a threshold of misclassification of one quartile, or a 25% change, we found that 920 patients, or 24.4% would be misclassified (**Table 2.1** and **Figure 2.4**). When looking only among those who moved, the change in score ranged from -98 to 96, with a standard deviation of 27 (**Figure 2.4**). Out of all those who moved, there were 443 pregnancies (11.7%), wherein the patient moved into a neighborhood at delivery that was at least 25% more deprived, and 477 pregnancies (12.6%) wherein the patient moved into an area that was at least 25% less deprived at delivery (**Table 2.2**). As illustrated by **Figure 2.4**, while most patients saw a small change in area deprivation, many patients did indeed see a large change in score. Mapping the Area Deprivation Index across the block groups of Philadelphia showed the degree of heterogeneity among neighborhoods within Philadelphia (**Figure 2.5**). We mapped the percent of patients who moved during pregnancy, aggregated by the census tract they were living in at time of delivery. This allowed us to visually note the misclassification that would occur across neighborhoods if residential mobility was not taken into account. Given the range of deprivation in Philadelphia, differential misclassification is a major concern (**Figure 2.5)**.

Table 2.1: Misclassification in a threshold of quartiles among patients who changed deprivation score (n = 3,774). The percent change in deprivation is inclusive of both positive and negative change.

		Pregnancies (N)	**Pregnancies (%)**
Overall Change in Deprivation (Both Positive and Negative Change)	**≥25 % change**	920	24.4
	≥50 % change	309	8.2
	≥75 change	84	2.2

Table 2.2: Downward and upward mobility seen in residential mobility during pregnancy, illustrating potential differential misclassification. Misclassification in quartiles among patients who changed deprivation score (n = 3,774)

		Pregnancies (N)	**Pregnancies (%)**
Change to More Deprived Area	**≥25 % change**	443	11.7
	≥50 % change	132	3.5
	≥75 change	36	1
Change to Less Deprived Area	**≥25 % change**	477	12.6
	≥50 % change	177	4.7
	≥75 change	48	1.3

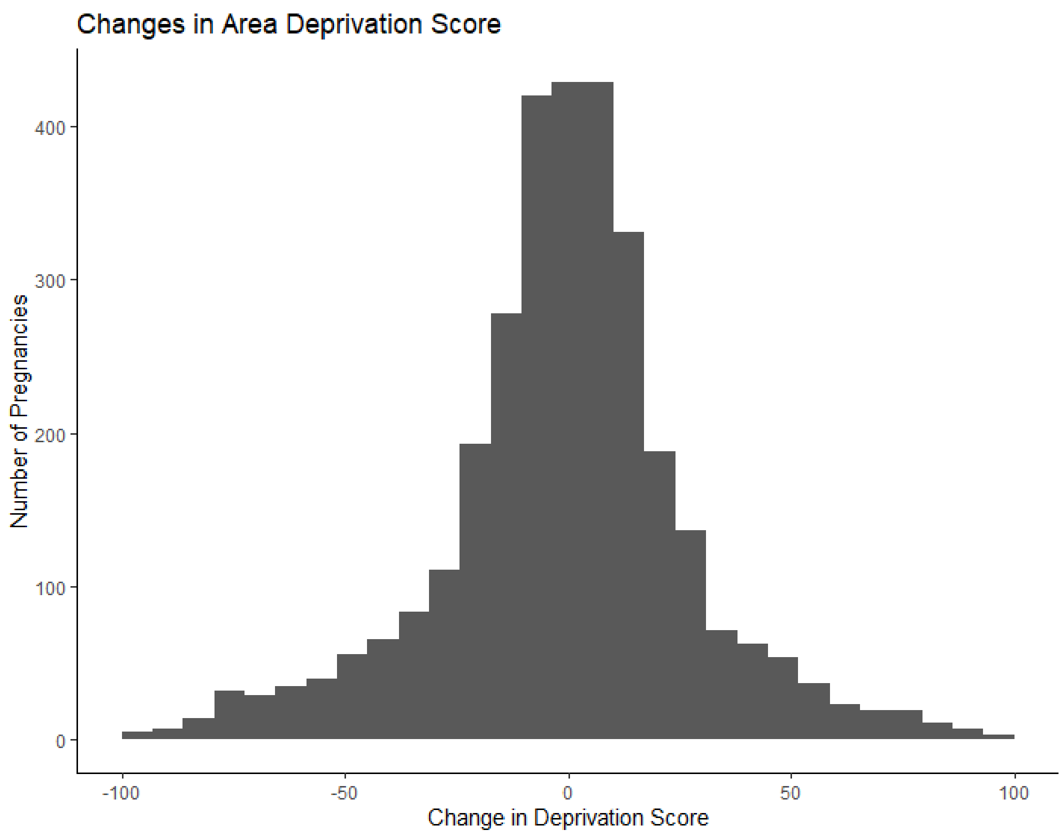

Figure 2.4: The distribution of the overall Area Deprivation Score, SD = 27

2.4. Discussion

2.4.1 Power of REMAP to solve a major misclassification of exposure problem

Our study tackles an important exposure characterization problem for environmental exposures assigned based upon residential addresses. To accurately identify patient moves or residential mobility, we developed REMAP, an automated algorithm to properly assign area level exposures from the Electronic Health Record (EHR) for large cohort studies. We found that REMAP was able to classify residential mobility with an accuracy of 95.7%.

In the literature there is an increasing recognition that residential mobility ought to be accounted for in epidemiologic studies so as to avoid the introduction of exposure misclassification (Canfield et al., 2006; Fell et al., 2004). However, some of the studies that have been done have used LexisNexis to construct residential histories, which is costly to use, and has variable accuracy of addresses depending on the beginning year of the time period of interest, the length of that study period, and the geographic area of the study (Jacquez et al., 2011; D. C. Wheeler & Wang, 2015). Further, in comparison to two recent studies that aimed to address this problem of exposure misclassification due to residential mobility, REMAP performs quite well. REMAP was able to correctly identify a patient's address change almost 96% of the time as compared to 69% (Fecht et al., 2020) and 72-90% (D. C. Wheeler & Wang, 2015). Overall, these results demonstrate that our residential mobility algorithm is able to be successfully run on a large EHR derived hospital cohort and classify whether a patient had moved or not, without needing the painstaking work of conducting chart review and manually determining whether a patient had moved.

2.4.2. Residential mobility events while pregnant

In our study population, we noted that about 41% of patients moved within a year prior to delivery. The available literature suggests that the average percentage of people who move during pregnancy is lower, between 10-30% (M. L. Bell & Belanger, 2012). It is possible that we see a higher number of people moving due to the urban location in which our population sits. There are a host of reasons why a person might move during pregnancy. These reasons might include, but are not limited to, needing more space, a safer neighborhood, proximity to family or friends, and the need to save money for the coming child. Why people choose to move, among the pregnant population or any other population is not something that can be ascertained without performing a qualitative study. As such, researchers who use REMAP in future studies will need to consider why their population might be more or less likely to move when contextualizing their results. Patients' likelihood to move may depend in part on their disease or condition status. For example, non-pregnant patients may be less likely to move. Therefore, researchers would have to take this into consideration when designing an environmental study that uses residential address information as a proxy for exposure.

2.4.3. Misclassification of area deprivation

As stated, without consideration of residential mobility, an exposure misclassification problem can occur. For instance, if a pregnant person is assigned an area deprivation score based upon an address on the date of delivery, but moved in the third trimester, the exposure for most of pregnancy would be misclassified. Our algorithm would pick up true changes in addresses between prenatal visits that are frequent enough to provide a reasonable assignment of a move date. In the pregnant population, many researchers are interested in understanding windows of susceptibility. Therefore, it is critical that the spatial exposures of interest are correctly classified. Without an algorithm to perform this function, manual review of addresses is necessary, which is time-consuming and costly. REMAP automates this process. However, to understand whether exposure classification would indeed occur, we utilized a validated national area, or neighborhood deprivation score as a proof of concept of REMAP. Without taking residential mobility into account, absolute misclassification of this deprivation exposure occurred in 39% of the patients in our cohort. However, when looking at a threshold of a 25% change in deprivation score, some relatively large changes were seen in pregnant patients with 24.4% being misclassified (**Table 2.1**). There was some evidence of differential misclassification seen among patients who moved into more deprived neighborhoods versus less deprived neighborhoods (**Table 2.2**). In addition, mapping the Area Deprivation Index in Philadelphia and the percentage of patients who moved per census tract (at delivery), illustrates the concern of differential misclassification when residential mobility is not taken into account and how this can differentially impact certain neighborhoods within a city more than others (**Figure 2.5**). If patients are moving more into deprived census tracts due to socio-economic constraints, rather than tracts with lower levels of deprivation, misclassification of the exposure would inherently be differential. Thus, utilizing

REMAP and taking residential mobility into account is crucial to avoid introducing this bias into longitudinal geo-spatial exposure studies.

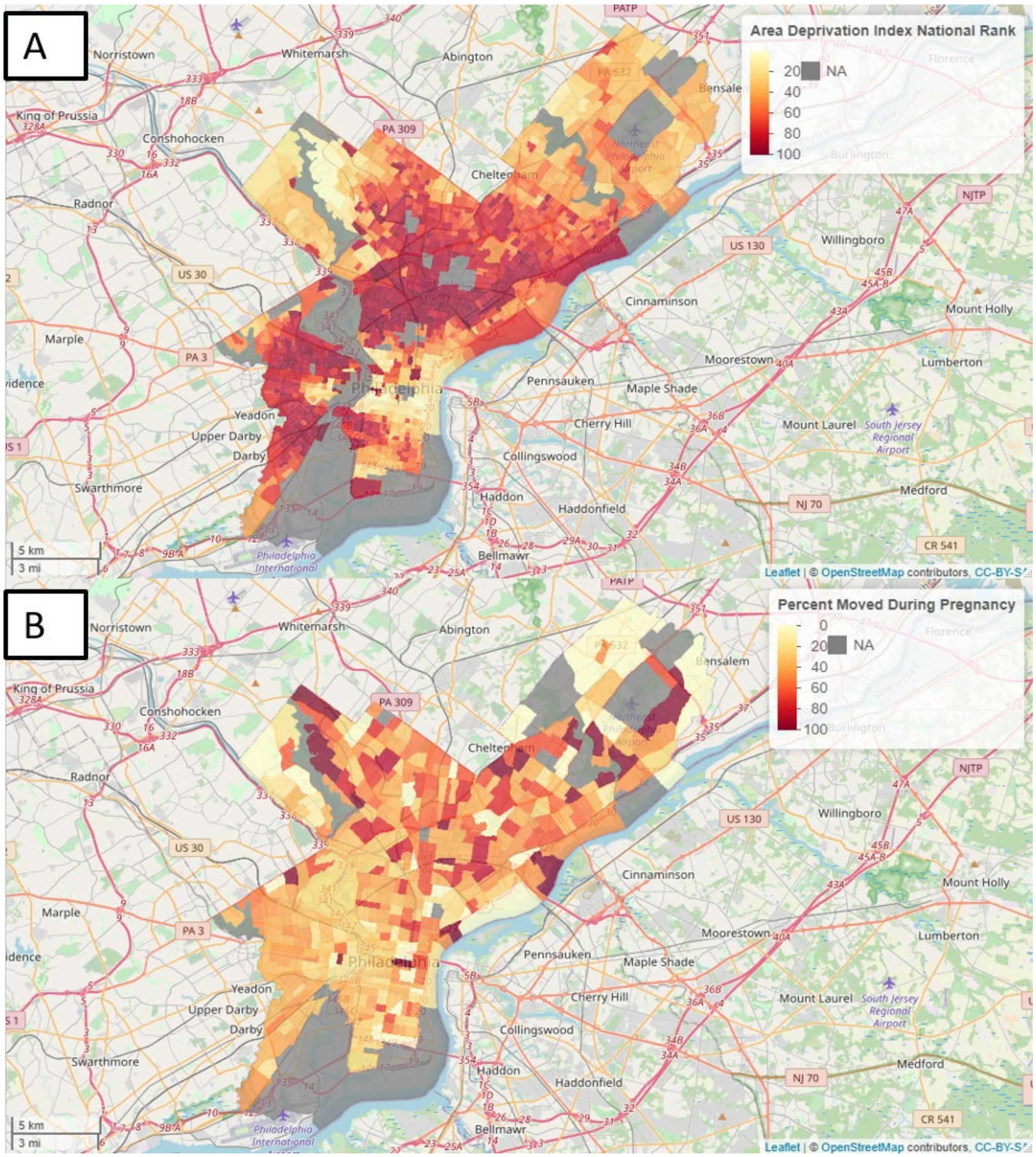

Figure 2.5: The Area Deprivation Index in Philadelphia (A) and the Percent of patients who moved during Pregnancy (B). Areas with Higher percentages of moved during pregnancy (Figure 6B) indicate areas where patients moved to during pregnancy. Therefore, using birth address only in analyses would result in greater misclassification for neighborhoods denoted in darker shades of red in Figure 6B (indicating greater percentages of moved patients in those neighborhoods).

2.4.4. Limitations of study

The address data we have is only as accurate as the data that is collected during a patient's visits in the year leading up to delivery. This can be affected by administrative entry errors, some of which we can account for in the algorithm. However, there are a host of reasons that a patient might not put down the address at which they live. Patients might report an old address, perhaps a parent's, where they still get their mail, or that they consider to be their permanent address. A patient might be living in a homeless shelter and therefore put a different address. They might put the address of the residence they rent or own but they may be spending the majority of their days at a partner's or family member's home. This misclassification of people's addresses would lead to some perpetuation of misclassification of the researcher's exposure of interest, potentially biasing our results. However, we propose it is still more likely to improve misclassification that occurs when not accounting for moving at all. Qualitative or survey methods that involve interviewing pregnant people who moved (within and across ZIP codes) would be required to understand address reporting as well as indications for moving.

2.5. Conclusions

In conclusion, we developed an algorithm called REMAP to classify whether a patient in a large Electronic Health Record (EHR) has moved or not. This algorithm provides a solution to the problem of exposure misclassification, even in a very large, error-prone EHR, reducing the need for manual review to determine whether a patient has moved. REMAP was 95.7% accurate, outperforming the comparison of ZIP codes alone (82.9% accuracy). In this large urban cohort, 41% of patients moved during pregnancy. Without taking residential mobility during pregnancy into account, we found that 24.4% of patients would be assigned a deprivation score misclassified by at least one quartile. In absolute terms, 39% of patients had a deprivation score that was misclassified at any level. Therefore, taking residential mobility into account is critical to the integrity of longitudinal geo-spatial epidemiology studies. The source code for this algorithm with dummy address data will first be made available via Github (https://github.com/bolandlab/REMAP) and, in the future we are planning to release an R package for other researchers who are working with address lists that they seek to compare for appropriate exposure classification.

CHAPTER 3: INDIDVIDUAL- AND NEIGHBORHOOD-LEVEL RISK FACTORS FOR SEVERE MATERNAL MORBIDITY

3.1. Background

Maternal morbidity and mortality persist as key indicators of women's health both globally and in the United States (US). While maternal mortality rates have been declining globally, they have concurrently increased in the US (Collaborators, 2016). Pregnancy-related deaths in the US have doubled from 7.2 to 18.0 deaths per 100,000 live births between 1987 and 2014 (Prevention). While mortality has steadily increased nationally, severe maternal morbidity (SMM) is 100 times more common in the US than maternal mortality (Creanga, 2017; A. A. Creanga et al., 2014). SMM includes unexpected, poor outcomes of labor or delivery that may result in short or long term consequences that are significant for the woman and her family (Prevention). National SMM rates have been reported by the Centers of Disease Control (CDC) since 1993 and up through 2014, using administrative hospital discharge data and International Classification of Diseases (ICD) diagnosis and procedure codes. SMM has risen by 75% over the last decade in the US, affecting over 52,000 women annually (Callaghan et al., 2012). As maternal morbidity continues to rise in the US, it is imperative that research be conducted to identify those at highest risk for SMM, so as to develop life-saving prevention strategies. Therefore, identifying risk factors for SMM is a critical step to this process.

Significant disparities persist in both SMM and maternal mortality. Research shows the risk of SMM and mortality are markedly increased among patients of color (H. H. Burris et al., 2019; Collaborators, 2016; N. Krieger et al., 1997). African American patients are upwards of four times as likely to die of complications from pregnancy versus White patients (Collaborators, 2016; Creanga, 2017; A. A. Creanga et al., 2014) and three times more like to suffer from an SMM compared to White patients (Fingar et al., 2018; Howell, Egorova, Balbierz, Zeitlin, & Hebert, 2016; Metcalfe, Wick, & Ronksley, 2018). In fact, a recent report from the Agency for Healthcare

Research and Quality found that Black patients had 10-fold increased risk of experiencing one of 21 SMM conditions compared to White patients (Fingar et al., 2018). Notably, individual factors alone such as medical comorbidities, maternal education or income do not explain this blatant disparity in SMM, highlighting the need for evaluation of additional risk factors that may contribute to these differences in outcomes. Krieger et al. have shown structural racism and historical segregation of neighborhoods to be huge drivers of poor health outcomes (Bailey et al., 2017; Nancy Krieger et al., 2020). It is in this vein of study that we hope to better understand the role of neighborhood disparities in SMM. Specifically, including Social Determinants of Health, or social and environmental stressors that can markedly affect women's health, is an understudied area in SMM research (Cabral et al., 1990; David & Collins, 1997).

The purpose of this study is to explore the role that individual risk factors (e.g., medical comorbidities) contribute to SMM while also exploring the contribution of neighborhood-level factors (e.g., poverty, violent crime, and housing violations) to SMM. By exploring both of these levels of risk factors, we can assess how strongly each level of stressors or covariates affects SMM in the diverse population served by the University of Pennsylvania Heath System (UPHS). Findings from our work will be helpful in future public health planning initiatives and clinical decision making to determine strategies to reduce SMM.

3.2. Methods

3.2.1. Data source and study population

The data used for this study comes from four hospitals within the University of Pennsylvania's Health System (UPHS), including the Hospital of the University of Pennsylvania (Philadelphia, PA), Chester County Hospital (West Chester, PA), Presbyterian Hospital (Philadelphia, PA), Pennsylvania Hospital (Philadelphia, PA), along with associated outpatient clinics. We identified deliveries from 2010 to 2017 from the EPIC Electronic Health Record (EHR) system using delivery diagnosis and procedure codes (Alur-Gupta, Boland, Sammel, Barnhart, & Dokras, 2019) and a previously developed algorithm (Canelón, Burris, Levine, & Boland, 2020). All patients with an identified delivery were included in the analysis and each delivery was analyzed independently.

3.2.2. Data ascertainment and SMM outcome definition

The International Classification of Diseases, ninth revision (ICD-9) and tenth revision (ICD-10) codes outlined by the Centers for Disease Control (CDC) for the indicators of SMM were utilized to characterize each inpatient delivery in the Electronic Health Record (EHR) for each patient in our cohort of deliveries within UPHS (Reproductive Health, 2019). We created the composite outcome of SMM by assessing whether each delivery was characterized by having at least one of the 21 SMM indicators outlined by the CDC (Callaghan et al., 2012; Prevention, 2019). We calculated SMM rates per 10,000 delivery hospitalizations. Rates of SMM were calculated with and without blood transfusion codes per the suggestion that the related ICD-9 and ICD-10 codes listed by the CDC had low specificity for hemorrhage (**Figure 3.1**) (Conrey et al., 2019; Main et al., 2016). The diabetes and preeclampsia covariates utilized in this study were obtained through ICD-9 and 10 coding within the EHR (**Table B.1**). As each patient may have had more than one delivery, a sensitivity analysis was performed randomly picking one pregnancy for the individual who had more than one.

3.2.3. Modeling of individual risk factors for SMM

Univariable and multivariable logistic regression models were constructed using all relevant and available potential individual risk factors for having a delivery characterized by an SMM. These factors included maternal age, race and ethnicity, marital status (married versus single), comorbidities (preeclampsia and diabetes), and other relevant delivery outcomes (cesarean delivery, stillbirth, preterm birth, multiple gestation). We used a forward step-wise approach for building parsimonious multivariable models, with an entrance and exit threshold of an alpha level of 0.2. These analyses were performed at the unit level of pregnancy. Subsequently, we performed a sensitivity analysis on a unique set of patients to insure that the assumption of independence of observations was not violated.

3.2.4. Spatial autoregressive model of neighborhood-level risk factors for SMM

We obtained neighborhood-level covariates at the census tract level from the United States Census Bureau and Open Data Philly, including poverty rate, violent and non-violent crime numbers, rate of housing violations, rate of owner vs. renter occupied housing, neighborhood median family income, percentage of women in the labor force, percentage of women receiving public assistance, and percentage of women who graduated high school. We also include at the neighborhood-level the percentage of those living in a neighborhood identifying as Black, Asian, or Hispanic (**Table B.2** and **Table 3.4**). We queried the census data using the Center for Enterprise Dissemination Services and Consumer Innovation interface. For this model we utilized 2017 data for our exposure (neighborhood-level covariates) and outcome (rate of delivery with an SMM for each census tract in Philadelphia with deliveries in UPHS). The specific American Community Survey (ACS) data file names that we used can be found in **Table B.2**. Open Data Philly was used for information on housing quality in Philadelphia. These data included law enforcement citations for buildings and units and housing quality law violations during inspections. Additionally, we utilized the Philadelphia Licenses and Inspections office violation data that contains unsafe and imminently dangerous housing violations in addition to general violations. Again, we used 2017 data to be consistent with the ACS data. Furthermore, we obtained 2017 data on violent and non-violent crime numbers, which originated from the Philadelphia Police Department (Balocchi & Jensen, 2019)**.** We performed univariable spatial regression analysis of neighborhood-level covariates on the rate of deliveries with an SMM per census tract (**Table 3.4**). Subsequently we performed backward selection with an exit threshold of a p-value of approximately 0.2 to create a final adjusted multivariable spatial regression model

(**Table 3.5**). These criterion were chosen so as to not exclude variables of importance with a very small alpha-level of 0.05, for example (Bursac, Gauss, Williams, & Hosmer, 2008). We built a spatial autoregressive model (Roger S. Bivand, 2013) for both the univariable and multivariable models due to a significant (p=0.04) Moran's I statistic, indicating the presence of spatial clustering with the outcome variable. The maximum likelihood estimate is reported for each covariate which represents the percent change in rate of SMM when multiplied by 100. A positive estimate is indicative of an increase in rate of SMM and a negative estimate is indicative of a decrease in rate of SMM.

We used R version 3.6.1 for all analysis. Major packages utilized for analysis include: dplyr (Hadley Wickham, 2020), ggplot2 (Wickham., 2016) , spdep (Bivand, 2018), spatialreg (Roger S. Bivand, 2013), and stats (R, 2019). The University of Pennsylvania's Institutional Review Board approved this study.

3.3. Results

Our cohort included 50,560 patients with delivery diagnoses or procedures at Penn Medicine and a total of 63,334 deliveries between 2010 and 2017, all of whom were included in the analyses for this study (Canelón et al., 2020). **Table 3.1** shows the demographic characteristics for the patients in our cohort. The average age at time of delivery was 29.48 and the average BMI was 31.8 kg/m^2. The predominant race descriptions were non-Hispanic Black or African American comprising 47.1% of pregnancies, and non-Hispanic White comprising 33.71% of pregnancies. Approximately 33% of the cohort had a cesarean birth and 11% had a preeclampsia diagnosis.

Table 3.1: Demographics for patients with 'delivery' at Penn Medicine Between 2010-2017		
Demographic	**Number of Deliveries (N = 63,334)**	**%**
Body Mass Index at time of Delivery (kg/m²)	Avg. 31.8 (SD: 12.5)	-
Age at time of Delivery (years)	Avg. 29.5 (SD: 6.1)	-
Marital Status		
Single	35,498	56.0%
Married	27,836	44.0%
Race/Ethnicity		
Hispanic	4,967	7.8%
American Indian or Alaskan Native	0	0.0%
Asian	160	0.3%
Black or African American	1,211	1.9%
Native Hawaiian or Other Pacific Islander	8	0.0%
White	3,403	5.4%
Other (includes other, unknown, mixed race, blank)	185	0.3%
Non-Hispanic	58,367	92.2%
American Indian or Alaskan Native	74	0.1%
Asian	3,910	6.2%
Black or African American	29,831	47.1%
Native Hawaiian or Other Pacific Islander	88	0.1%
White	21,349	33.7%
Other (includes other, unknown, mixed race, blank)	3,115	4.9%
Cesarean delivery	20,894	33.0%
Stillbirth	516	0.8%
Multiple Gestation	1,562	2.5%
Preterm Birth	3,897	6.2%
Diabetes	2,687	4.2%
Preeclampsia	6,779	10.7%

3.3.1. Overall SMM rate

We found the overall SMM rate from 2010-2017 to be 2.73%, or 272 deliveries with SMM per 10,000 delivery hospitalizations. **Table 3.2** shows the individual indicators of the SMM and their frequencies among all of the deliveries in our cohort, the number per 10,000 delivery hospitalizations and the percentage that each individual indicator contributes to the overall SMM. The most frequent SMM indicator was blood products transfusion, occurring in 1.73% of all deliveries and accounting for 63.5% of SMM deliveries. When excluding blood transfusions, the overall SMM rate was 1.3% or 130 deliveries with SMM per 10,000 delivery hospitalizations (**Table 3.2**). The distribution of frequency of the SMM indicators are noted in **Figure B.1**. **Figure 3.1** demonstrates the rate of SMM over time from 2010 through 2017. The rate of SMM per 10,000 deliveries decreased markedly in 2016 (orange line) when using the SMM definition that includes blood transfusions. As noted in the figure, this is due to a marked reduction in the rate of blood transfusions (gray line). When excluding blood transfusions, the annual SMM rate per 10,000 hospital deliveries remained relatively stable from 2010-2017.

Table 3.2: Severe maternal morbidity (SMM) indicators (n) out of 63,334 delivery hospitalizations				
Indicator	**(N)**	**% of 63,334 delivery hospitalizations**	**N per 10,000 delivery hospitalizations**	**% of 1,726 SMM Deliveries**
Blood Products Transfusion	1096	1.73%	173.1	63.5%
Disseminated Intravascular Coagulation (DIC)	284	0.45%	44.8	16.5%
Acute renal failure	167	0.26%	26.4	9.7%
Pulmonary edema/Acute heart failure	84	0.13%	13.3	4.9%
Sepsis	62	0.10%	9.8	3.6%
Hysterectomy	61	0.10%	9.6	3.5%
Eclampsia	61	0.10%	9.6	3.5%
Ventilation	57	0.09%	9.0	3.3%
Air and Thrombotic Embolism	49	0.08%	7.7	2.8%
Puerperal cerebrovascular disorders	48	0.08%	7.6	2.8%
Shock	47	0.07%	7.4	2.7%
Adult respiratory distress syndrome	44	0.07%	6.9	2.5%
Sickle cell disease with crisis	41	0.06%	6.5	2.4%
Temporary Tracheostomy	36	0.06%	5.7	2.1%
Severe anesthesia complications	15	0.02%	2.4	0.9%
Heart failure/arrest during surgery or procedure	10	0.02%	1.6	0.6%
Conversion of cardiac rhythm	8	0.01%	1.3	0.5%
Aneurysm	6	0.01%	0.9	0.3%
Cardiac arrest/ventricular fibrillation	5	0.01%	0.8	0.3%
Amniotic Fluid Embolism (AFE)	2	0.00%	0.3	0.1%
Acute myocardial infarction	2	0.00%	0.3	0.1%
TOTAL Deliveries with an SMM	1726	2.73%	272.5	
TOTAL Deliveries with an SMM excluding blood transfusions	825	1.30%	130.3	
Average number of indicators per delivery: 0.033 (Range: 0-10)				
Average number of indicators per SMM delivery: 1.26 (Range: 1-10)				

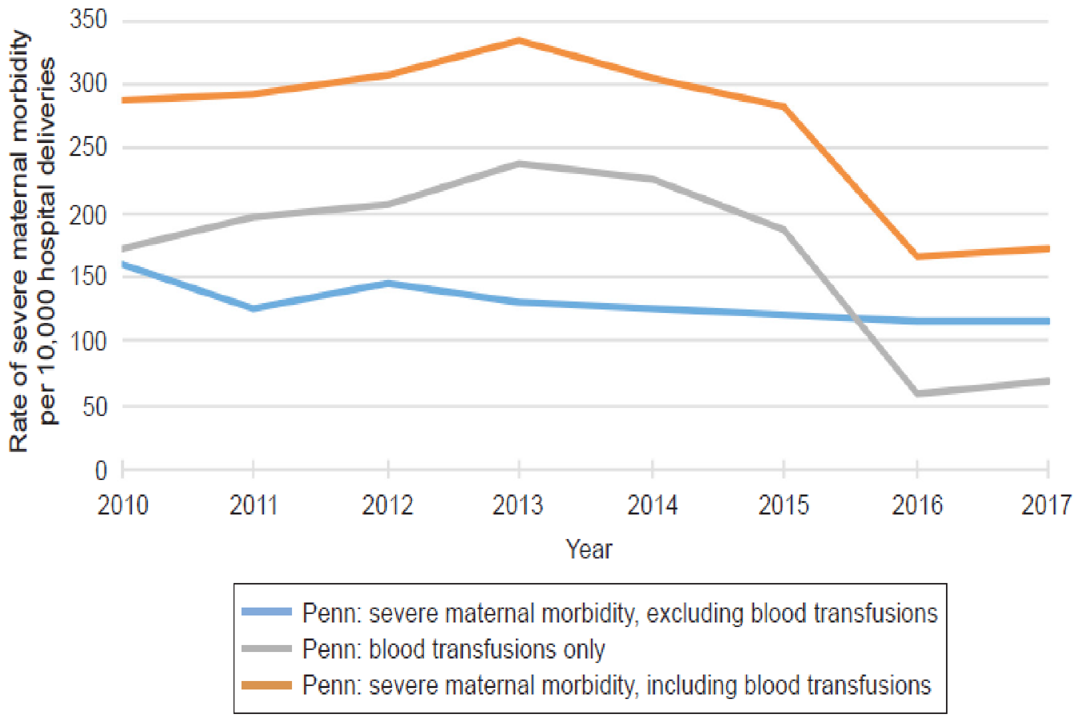

Figure 3.1: The trend in rate of SMM including blood transfusions, excluding blood transfusions, and rate of blood transfusions alone, per 10,000 delivery hospitalizations in the University of Pennsylvania Hospital System from 2010-2017.

3.3.2. Individual-level risk factors for SMM

We assessed the univariable and multivariable association between the patient-level variables and delivery with SMM. As noted in **Table 3.3**, there were multiple individual-level covariates associated with SMM in the univariable analysis. However, on adjusted analysis only race, cesarean delivery, stillbirth, multiple gestation, preterm birth and preeclampsia were noted to be significant independent risk factors for SMM. The magnitude of risk was highest for cesarean delivery (aOR 3.50, 95% CI 3.15-3.89), stillbirth (aOR 4.60, 95% CI 3.31-6.24) and preeclampsia (aOR 2.71, 2.41-3.03). Notably, White race was the only individual characteristic that was associated with a lower odds of SMM at delivery (aOR 0.73, 95% CI 0.61-0.87). The 63,334 pregnancies in our cohort were from 50,560 unique patients. Because some women gave birth more than once, the assumption of independent observations for logistic regression may not hold. With that in mind, we reran the analysis with only one pregnancy for patients who had multiple births and found that the effect sizes did not differ by more than 10% (**Table B.3** and **Table 3.3**).

Table 3.3: Individual risk factors for severe maternal morbidity - univariable and multivariable Analysis

Risk Factor	OR	95% CI	aOR	95% CI
Race/Ethnicity				
Hispanic	0.89	0.73-1.07		
Non-Hispanic				
Black or African American	1.34	1.22-1.48	1.10	0.95-1.29
White	0.68	0.61-0.76	0.73	0.61-0.87
Asian	1.23	1.02-1.48	1.43	1.04-1.63
American Indian or Alaskan Native	1.61	0.39-4.33		
Hawaiian or Pacific Islander	0.87	0.81-1.29		
Other	1.02	0.85-1.34		
Age	1.01	1.00-1.02		
Weight	1.00	1.00-1.00		
Height	1.00	0.97-1.03		
BMI	1.00	0.99-1.00		
Cesarean delivery	3.72	3.36-4.12	3.50	3.15-3.89
Stillbirth	3.82	2.79-5.12	4.60	3.31-6.24
Multiple gestation	2.51	2.01-3.08		
Preterm birth	2.20	1.89-2.55	1.65	1.41-1.93
Diabetes	1.46	1.18-1.78		
Preeclampsia	3.53	3.16-3.93	2.71	2.41-3.03

3.3.3. Spatial autoregressive modeling with neighborhood-level covariates

We conducted univariable and multivariable spatial regression modeling with the neighborhood-level covariates (**Table B.2 and Table 3.4)** and rate of deliveries with SMM per each census tract with deliveries in Philadelphia. **Figure B.2** depicts a map of the percent of deliveries with SMM out of the total deliveries per each census tract in Philadelphia. As illustrated in **Table 3.4**, multiple neighborhood-level covariates were associated with an increased rate of SMM in the univariable analysis. Specifically, there was an increased rate of SMM in the univariable analysis for people living in neighborhoods with: higher percentage of people who self-identify as Black or African American, a higher number of violent crimes, a higher percentage of renter-occupied housing units, higher number of housing violations, higher percentage of reproductive age women who graduated high school, and a higher percentage of women receiving public assistance. There was a lower rate of SMM for people living in neighborhoods with a higher percentage of people who self-identify as White or Asian, and a higher median income. Estimates for **Table 3.4** are included in Appendix B (**Table B.4**).

Three of the neighborhood-level covariates were retained in the final multivariable model (**Table 3.5**) including percentage of the census tract identifying as Black or African American, the census tract number of violent crimes (log-transformed), and percentage of the census tract identifying as White. Specifically, there was a 2.4% increase in SMM rate for a ten percent increase in census tract identifying as Black or African American, when adjusting for the number of violent crimes (log-transformed) and percentage of people who identify as White (95% CI 0.37-4.4). Additionally, there was a 3% increase in SMM rate for a one unit increase in the log-transformed number of violent crimes when adjusting for the percentage of those who identify as Black or African American and White (p-value = 0.06). Estimates for this model are included in Appendix B (**Table B.5**)

Table 3.4: Results of Univariable Spatial Regression Analysis of Neighborhood-Level Covariates on Percent of Deliveries with an SMM per Census Tract		
Neighborhood-Level Covariate	**% Change in SMM Rate***	**95% CI**
Percent of each census tract that identifies as **Black or African-American** Alone	0.15	0.08-0.22
Percent of each census tract that identifies as **White** Alone	-0.15	0.07--0.23
Number of Violent Crimes (log-transformed variable)	4.90	2.02-7.83
Percent of occupied housing units in each census tract that are **renter**-occupied	0.05	-0.09-0.19
Housing Violations (log-transformed variable)	3.90	1.40-6.21
Percent of women aged 15-50 years in each census tract that **graduated high school** (including equivalency)	0.29	0.10-0.47
Percent of each census tract that identifies as **Asian** Alone	-0.33	-0.63-0.03
Percent of women aged 15-50 years in each census tract that **received public assistance** income in the past 12 months	0.40	0.01-0.79
Percent of women aged 15-50 years in each census tract below 100 percent **poverty** level	0.11	-0.03-0.25
Percent of each census tract that identifies as **Hispanic or Latinx**	-0.08	-0.23-0.05
Number of Non-Violent Crimes (log-transformed variable)	2.00	-1.8-5.9
Percent of occupied housing units in each census tract that are **owner**-occupied	-0.05	-1.9-0.09
Percent of women aged 16-50 years in each census tract that are **in the labor force**	-0.05	-0.24-0.14
*Percent change in the rate of SMM per a one unit-increase in neighborhood-level covariate		

Table 3.5: Results of multivariable spatial regression analysis of neighborhood-level covariates on percent of deliveries with a severe maternal morbidity (SMM) per census Tract		
Neighborhood-Level Covariate	**% Change in SMM Rate***	**95% CI**
Percent of each census tract that identifies as **Black or African-American** Alone	0.24	0.04-0.44
Number of Violent Crimes (log-transformed variable)	3.0	-0.15-6.8
Percent of each census tract that identifies as **White** Alone	0.15	-0.09-0.38

*Percent change in the rate of SMM per a one unit-increase in neighborhood-level covariate

3.4. Discussion

We studied individual- and neighborhood-level risk factors of SMM and explored the contributing factors of each on the risk of SMM. The individual-level risk factors with the highest magnitude of increased adjusted odds of SMM included: having a cesarean delivery, a stillbirth, or a preeclampsia diagnosis. Furthermore, census tracts with a higher percentage of Black or African Americans and census tracts with a higher rate of violent crime had higher rates of SMM.

Although the effect of individual-level factors on SMM has been studied widely (Callaghan et al., 2012; Andreea A Creanga et al., 2014), we are uniquely positioned to investigate the role of these factors among patients of color due to our racially diverse cohort of patients. Unlike individual-level factors, prior research on the impact of neighborhood-level factors on SMM are limited and conflicting. While some found racial composition of neighborhoods and poverty to be a significant neighborhood-level risk factor, others did not (Guglielminotti, Landau, Wong, & Li, 2019; Howland et al., 2019; Janevic et al., 2020). Our findings support those of Janevic *et al.* and Howard *et al,* which showed spatial racial and economic polarization of neighborhoods and living in poverty to be significantly associated with rates of SMM (Howland et al., 2019; Janevic et al., 2020).

Specifically, in our univariable analysis the rate of SMM increased by 1.5% as neighborhoods had a ten percent increase in percentage of Black or African-American identifying patients. Additionally, the rate of SMM was lowered by 1.5% with every ten percent increase in percent of patients identifying as White. These results may be indicative of the historic or present-day effects of racial and ethnic segregation within Philadelphia neighborhoods. In fact, in the US, African Americans remain the most segregated racial or ethnic group, and as such it is estimated that more than 60% of urban dwelling African-Americans would need to move in order to achieve a non-segregated geographic distribution (J. F. Bell, Zimmerman, Almgren, Mayer, & Huebner, 2006). A number of studies have been done that illustrate the deleterious effect of racial segregation on birth outcomes due to undue stress on the mother (J. F. Bell et al., 2006; N. Krieger, Waterman, et al., 2017; Mehra et al., 2017). Crime, another known cause of stress, was also noted to be associated with SMM in our data. When adjusting for the log-transformed number of violent crimes and percent of each census tract that identifies as White alone, we saw the rate of SMM increase by 2.4% for every ten percent increase in those who identify as Black or African American alone (95% CI 0.37-4.4). While Howland *et al.* found a strong association between living in impoverished neighborhoods and SMM, we failed to find neighborhood-level poverty to be a risk factor for delivery with SMM in our multivariable model; however, we did find violent crime to be positively associated. It is possible that our failure to find an association between SMM and poverty is because poverty and violent crime may be so closely correlated in our cohort that modeling only finds violent crime to be the predominant driver. Violent crime is a known risk factor for adverse pregnancy outcomes (Masi, Hawkley, Piotrowski, & Pickett, 2007; Messer, Kaufman, Dole, Savitz, & Laraia, 2006). Screening for neighborhood-level crime could be considered for risk-based severe maternal morbidity screening; however, we must be cognizant to not perpetuate biases that are not biological in nature.

Our study has both strengths and limitations. Our diverse cohort is majority patients of color, allowing us the ability to investigate the role of race on delivery with SMM, a known driver of disparate outcomes. We therefore would expect our results to be generalizable to other diverse, urban populations. Additionally, we utilized a validated algorithm to identify deliveries within our health system, ensuring we accurately captured all patients and thereby allowing for a large sample size in which to evaluate SMM. While the use of composite outcomes has its limitations, the CDC SMM composite outcome (used in this study) is a well-established SMM outcome to evaluate, and specifically allows us to compare our data to that of national CDC data. When doing that, it is notable that our rate of SMM was higher than the rate reported by the CDC: 159, 130, and 125 per 10,000 deliveries for UPHS (excluding blood transfusions) vs. 33, 34 and 35 per 10,000 deliveries for the CDC (excluding blood transfusions) in 2010, 2013, and 2014, respectively (**Figure 3.2**). This may be due, in part, to the high-risk, diverse patient population delivering within the UPHS system with a large number of underlying medical comorbidities. Lastly, there are always limitations that come from utilizing EHR data, as it is reliant on coding for billing purposes and is therefore subject to misclassification and lack of availability of all covariates of interest. For example, we were unable to include variables such as parity in our models as data were not available specifically for that covariate. Additionally, our study spans 2010-2017, during which time billing codes transitioned from ICD-9 to ICD-10. Diagnosis and procedural codes became more granular with the introduction of ICD-10 codes in 2015 and therefore possible misclassification for variables, e.g. blood transfusions could occur. The decreased rate of blood transfusions noted in 2016 was less likely due to clinical differences in the actual rate of blood transfusion and more likely due to over estimation in the years prior to ICD-10 coding (Callaghan et al., 2012).

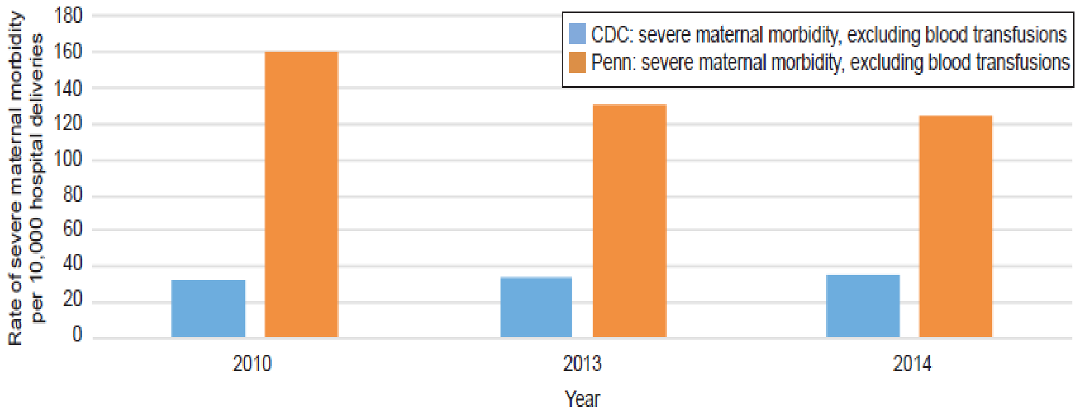

Figure 3.2: The rate of SMM per 10,000 delivery hospitalizations (excluding blood transfusions) in the University of Pennsylvania Hospital System and the United States (per the CDC) in 2010, 2013 &2014.

3.5. Conclusions

In conclusion, this study furthers the research being done on nationally rising rates of SMM, one of the most significant contributors to poor health outcomes for women (Geller et al., 2018). As seen in the literature, we found that certain individual-level characteristics increase one's likelihood of experiencing an SMM. Namely, being non-White, having a cesarean delivery, a stillbirth, multiple gestation or preeclampsia increase the risk of SMM. Equally as important however, neighborhood level factors also appear to be important drivers of SMM and suggest that perhaps historic and present-day structural racism and violent crime play a role in rates of SMM. This study's approach to interrogating both individual- and neighborhood-level covariates is a holistic approach to identifying places for clinical and public health interventions to help explain some of the racial or ethnic differences in risk of SMM, along with the other known comorbidities of SMM. This study importantly highlights, once again, that differences in SMM by race are biological or due to clinical risk factors alone. With the neighborhood-level factors we found to be independent predictors of SMM, differences in race and SMM are more likely to be due to the social-construct of race and racism itself. Characterizing the risk factors of SMM is imperative for the design of clinical and public health interventions that seek to lower rates of SMM and maternal mortality.

CHAPTER 4: NEIGHBORHOOD DEPRIVATION INCREASES THE RISK OF POST-INDUCTION CESAREAN DELIVERY

4.1. Background

Among the over 3.7 million pregnant people who give birth in the United States annually, more than 20% of them will experience a labor induction, making induction one of the most common procedures done during pregnancy (Hamilton, 2020; "Recent declines in induction of labor by gestational age," 2016; *WHO recommendations for induction of labour*, 2011). Of these inductions, about one third will end in a cesarean delivery (Rouse et al., 2011; Vahratian, Zhang, Troendle, Sciscione, & Hoffman, 2005). While the definition of a “failed induction” is not as simple as a cesarean delivery after labor induction (Grobman et al., 2018), a vaginal delivery is often the preferred outcome by delivering patients. There are many identifiable risk factors for cesarean delivery such as hypertension, obesity, parity, and gestational age, however one plausible risk factor with limited evaluation to date is neighborhood deprivation. Neighborhood deprivation is a measure of a neighborhood's overall access to resources, with high levels of deprivation indicating low access to income, education, and other resources. Additionally, neighborhood deprivation has been associated with poor health outcomes such as cancer (Mora et al., 2020) and Alzheimer’s disease (Powell et al., 2020) and has been associated with adverse pregnancy outcomes including pregnancy-induced hypertension and preterm birth (Vinikoor-Imler, Messer, Evenson, & Laraia, 2011). Therefore we sought to evaluate the link between neighborhood deprivation and post-induction cesarean delivery.

Patients of color disproportionately undergo cesarean delivery in the United States. Even when controlling for sociodemographic factors and medical comorbidities, Black patients have a 50% increased odds of cesarean delivery when compared to White patients (Moaddab et al., 2018; Stark, Grobman, & Miller, 2019). We know that these persistent disparities are not genetic in nature, but rather arise from a complex system of elements that include provider-, hospital-, and geographic-level factors that lead to large variations in cesarean delivery rates by race. Longstanding racial residential segregation leads to large differences in neighborhood environmental exposures by race in the United States (Heather H Burris & Hacker, 2017; Mehra et al., 2017). Indeed, a recent paper by Nardone *et al.* illustrates the deleterious effect of redlining on birth outcomes (Nardone et al., 2020). Given the interaction of environmental stressors with hormonal pathways (Harris & Seckl, 2011; Henson & Chedrese, 2004; Mehra et al., 2017; Patisaul & Adewale, 2009; Whirledge & Cidlowski, 2010), it is biologically plausible that patients from areas of neighborhood deprivation may respond more or less favorably to labor induction. Because differences in cesarean delivery outcomes cannot be attributed to sociodemographic factors and patient comorbidities alone, we must evaluate novel risk factors for increased cesarean risk, such as neighborhood deprivation.

While approximately one third of labor inductions do end in cesarean deliveries, the ability to predict who will have a vaginal delivery after labor induction has been limited (Grobman, 2012; Tolcher, 2020; Vahratian et al., 2005). An exception is the work of Levine *et al.,* whose team was able to create a successful risk prediction model for cesarean delivery after induction (Hamm, Downes, Srinivas, & Levine, 2019). While they, and others, have investigated patient-level risk factors such as height, BMI, parity, cervical examination findings, and gestational age to estimate risk of cesarean after labor induction (Hamm et al., 2019; Levine et al., 2018), studies of the role of neighborhood-level exposures, such as neighborhood deprivation, on labor induction outcome are lacking.

The aim of this study is to evaluate the contribution of neighborhood deprivation on risk of cesarean delivery after labor induction.

4.2. Methods

Our study population included patients who had a pregnancy-related delivery diagnosis and procedure codes in their University of Pennsylvania Health System (UPHS) EPIC Electronic Health Record (EHR) system (Alur-Gupta et al., 2019; Canelón et al., 2020) from 2010 to 2017 as well as an International Classification of Diseases versions 9 and 10 codes (ICD-9 and ICD-10) for labor induction validated by the American College of Obstetrics and Gynecologists (**Table C.1**) (Collaborative). We then linked our data with detailed birth logs obtained from two hospitals within UPHS, the Hospital of the University of Pennsylvania (Philadelphia, PA) and Pennsylvania Hospital (Philadelphia, PA) (Boland, Alur-Gupta, Levine, Gabriel, & Gonzalez-Hernandez, 2019). We included all patients who delivered at term (≥37 weeks) with a live, singleton gestation. We excluded patients with a prior cesarean captured in the EHR and patients lacking address information precluding geocoding. All individual covariates, such as pregnancy related hypertension and diabetes, used in this study were defined using ICD-9 and ICD-10 codes. We also identified clinically recognized obesity as those with obesity-related ICD-9 and ICD-10 codes. For patients with more than one delivery within our health system during the study period, we randomly chose one pregnancy in order to achieve independence between deliveries.

The primary outcome for this study was post-induction cesarean delivery for any indication, which was determined using ICD-9 and ICD-10 codes for cesarean delivery. The primary exposure of interest was neighborhood deprivation. We chose to utilize the University of Wisconsin's Neighborhood Atlas Area Deprivation Index (ADI), composed of 17 education, employment, housing-quality and poverty measures from long-form Census data and American Community Survey (ACS) data. We used the ADI national rank score for the US, which ranges from 1-100, with a score of 100 being the highest level of deprivation in the US and a score of one being the lowest (Kind & Buckingham, 2018). We assigned an ADI score for each of the geocoded, block group geoids based on the latitudes and longitude of address at delivery. For each delivery, we binned the change in deprivation score into four levels: lowest deprivation (ADI score of 0-24), moderate deprivation (ADI score of 25-49), high deprivation (an ADI score of 50-74), and highest deprivation (an ADI score of 75-100) using evenly spaced deprivation score categories. Binning of neighborhood deprivation into high vs. low categories is commonly done in the literature as it increases interpretability of the results (Mora et al., 2020; Powell et al., 2020) .

We utilized a generalized linear mixed model for univariable and multivariable modeling. We first modeled the univariable association between the neighborhood deprivation levels and post-induction cesarean delivery. Based on clinical knowledge and plausibility, gestational age and parity were chosen *a priori* to be included in the multivariable model, regardless of their significance. We then sought to assess the level of confounding for the additional remaining individual-level covariates, including: pregnancy-related hypertension, diabetes, obesity, marital status, race/ethnicity, and patient age at time of delivery. We evaluated whether these variables confounded the association of neighborhood deprivation and cesarean delivery by adding them individually into the univariable model of neighborhood deprivation and post-induction cesarean delivery and assessing whether the most significant effect size for the association between ADI categories and post-induction cesarean delivery changed by about 10%. Based upon these determinations for confounding we built a parsimonious multivariable model. We then added back in the other variables to check to see if they further confounded the association. Those that did were then added into the multivariable model.

Our multivariable mixed level model included a random effect for neighborhood to account for neighborhood clustering. As a secondary analysis we also modeled neighborhood deprivation as a non-linear spline, allowing for greater flexibility of the variable in modeling the association with post-induction cesarean.

We used R version 3.6.1 for all analysis. Major packages utilized for analysis include: tidyverse (Wickham & https://CRAN.R-project.org/package=tidyverse, 2017), dplyr (Hadley Wickham, 2020), stats (R, 2019), mgcv (Wood, 2011), cowplot (Wilke, 2019) and ggplot2 (Wickham., 2016). The University of Pennsylvania's Institutional Review Board approved this study.

4.3. Results

We derived a cohort of 63,334 pregnant patients from the University of Pennsylvania health system (Canelón et al., 2020). We linked this with a birth log cohort obtained from the Hospital of the University of Pennsylvania and Pennsylvania Hospital from 2010-2017 resulting in a cohort of 35,787 patients. After applying our inclusion and exclusion criteria, 24% of these patients remained in our final cohort of 8,672 inductions. The post-induction delivery outcomes included 2,027 cesarean deliveries (23%) and 6,645 vaginal deliveries (77%) (**Figure 4.1**) The average patient age at time of delivery was 28.4 ± 6.2 years. The predominant race self-designations were Black or African American, comprising 58% of patients, and White, 30% of patients. The majority of patients reported their marital status as single (64%). In this cohort, 5% of patients had diabetes, 18% had pregnancy-related hypertension, and 22% were clinically coded as obese (**Table 4.1**).

We found that living in neighborhoods with moderate, high and highest levels of neighborhood deprivation resulted in elevated aORs for post-induction cesarean delivery compared to the lowest level of neighborhood deprivation. The odds of post-induction cesarean delivery were elevated by 29% for the highest-level of deprivation (95% CI 1.05-1.57), 28% for the second highest-level (95% 1.04-1.57), and 20% for the third highest or moderate-level (1.00-1.44) (**Table 4.2**). The random effect for neighborhood clustering was not significant at an alpha-level of 0.05 (p-value = 0.64). Unadjusted or crude ORs are also presented in **Table 4.2**, but are less clinically meaningful. Our models adjusted for individual-level confounders for post-induction cesarean delivery including parity, gestational age, disease-status (obesity, diabetes, and pregnancy-related hypertension), patient age, race/ethnicity, and marital status.

We included race/ethnicity at the individual level in our full adjusted model of neighborhood deprivation on post-induction cesarean delivery. We included this important individual-level factor not because we believe that race/ethnicity plays a biological role in the association but to account for other factors of racism that are not captured via neighborhood deprivation. Race/ethnicity did change the most significant effect size by greater than 10%, and thus we included it in the model despite our belief that race/ethnicity's influence on post-induction cesarean delivery is not biological in nature, but rather due to systemic racism.

Our secondary analysis modeling neighborhood-deprivation as a non-linear spline also showed an increase in odds of post-induction cesarean delivery with increased neighborhood deprivation (**Figure 4.2**). We include this analysis to show that neighborhood deprivation and post-induction cesarean delivery are largely linearly related and not purely dependent on how we binned neighborhood deprivation levels in 4-categories. Lastly, we conducted a sensitivity analysis by running this multivariable model on a sub-population for whom we have residential mobility data, as defined by an address change within one-year prior of delivery. By including residential mobility in the model in this sub-group, the effect sizes for neighborhood-deprivation are increased across all levels (**Table C.2**). A table with the results from each of the three models is included in the appendix (**Table C.3**).

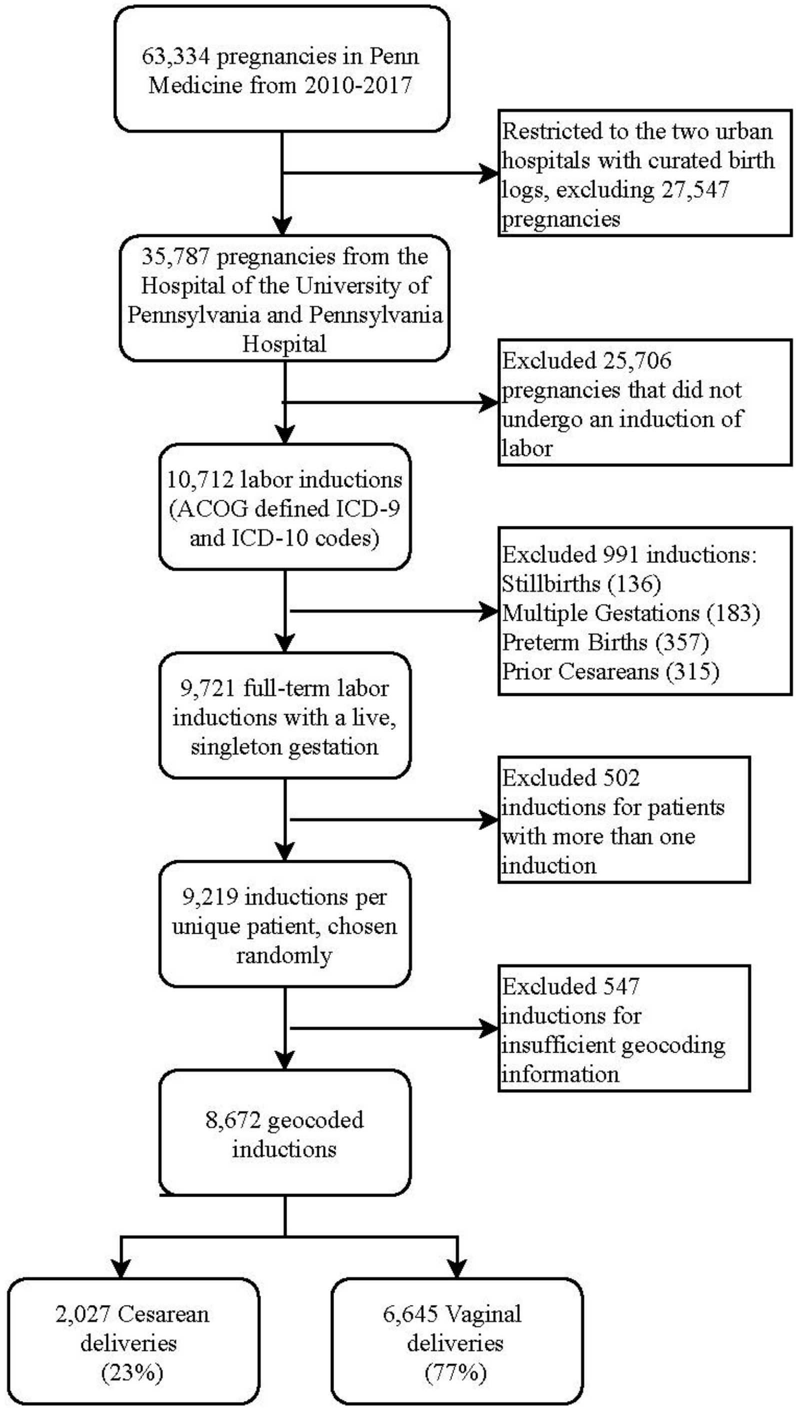

Figure 4.1: Flow diagram showing final cohort composition, including exclusions and percentage of cesarean deliveries and vaginal deliveries after labor induction.

Table 4.1: Demographics for patients* who underwent a labor induction between 2010-2017				
Demographic	**Total Labor Inductions (n = 8,672) n(%)**	**Cesarean (n=2,027) n(%)**	**Vaginal (n=6,645) n(%)**	**p-values**
Neighborhood Deprivation				
Highest (75-100)	3863 (45)	865 (43)	2988 (45)	0.05
High (50-74)	1637 (19)	399 (20)	1238 (19)	
Moderate (25-49)	1508 (17)	387 (19)	1121 (17)	
Lowest (0-24)	1664 (19)	376 (19)	1288 (20)	
Marital Status				
Single	5534 (64)	1301 (64)	4233 (64)	0.71
Married	3138 (36)	726 (36)	2414 (36)	
Age at time of Delivery (years)	Mean 28.4 (SD: 6.2)	Mean 28.8 (SD: 6.5)	Mean 28.4 (SD: 6.1)	0.01
Ethnicity				
Hispanic (versus non-Hispanic)	547 (6)	128 (6)	419 (6)	1.00
Race				
American Indian or Alaskan Native	8 (0)	2 (0)	6 (0)	0.51
Asian	567 (7)	145 (7)	422 (6)	
Black or African American	5023 (58)	1165 (58)	3858 (58)	
Native Hawaiian or Other Pacific Islander	9 (0)	4 (0)	5 (0)	
White	2626 (30)	606 (30)	2020 (30)	
Unknown	164 (2)	44 (2)	120 (2)	
Other	275 (3)	61 (3)	214 (3)	
Diabetes (versus no diabetes)	439 (5)	122 (6)	317 (5)	0.03
Pregnancy-related hypertensions (versus not)	1528 (18)	470 (23)	1058 (16)	<0.001
Obesity (versus not obese)	1969 (22)	626 (31)	1343 (20)	<0.001

*for patients with multiple pregnancies, a pregnancy was chosen at random to ensure that each patient is represented only once in the model
Data presented as n (column %) unless otherwise specified.

Table 4.2: Associations between neighborhood deprivation and cesarean delivery following labor induction

Covariate	Cesarean rate	Crude OR	95% CI	Adjusted OR[a]	95% CI
Neighborhood Deprivation					
Highest (75-100)	22.39%	0.90	0.78-1.03	1.29	1.05-1.57
High (50-74)	24.37%	1.07	0.91-1.26	1.28	1.04-1.57
Moderate (25-49)	25.66%	0.91	0.77-1.06	1.20	1.00-1.44
Lowest (0-24)	22.60%	1.00	Reference	1.00	Reference
Comorbidities					
Diabetes (versus no diabetes)	27.79%	1.30	1.03-1.58	1.10	0.85-1.43
Pregnancy-related hypertensions (versus not)	30.76%	1.59	1.41-1.80	1.70	1.47-1.97
Obesity (versus not obese)	31.79%	1.76	1.58-1.97	1.95	1.70-2.23

[a]Additionally adjusted for maternal age (continuous), race/ethnicity, parity, gestational age, and marital status

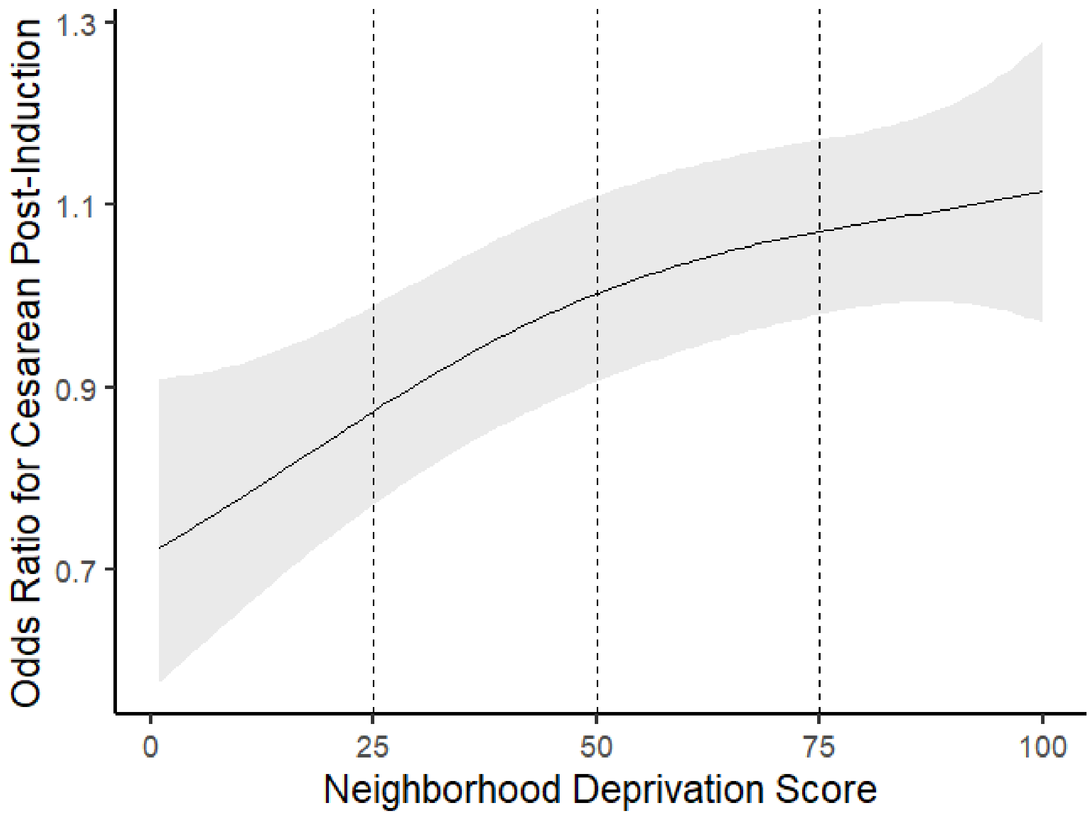

Figure 4.2: Association between neighborhood deprivation and odds of cesarean delivery after induction. Model adjusted for parity, gestational age, race/ethnicity, patient age, obesity, pregnancy-related hypertension, diabetes, and marital status, with a random effect for neighborhood. Each point on the curve is the OR for people with that neighborhood deprivation score compared to all other patients. Vertical dashed lines represent the binning of deprivation score in the primary generalized linear mixed model analysis.

4.4. Discussion

We studied the effect of neighborhood deprivation on post-induction cesarean delivery, accounting for individual level characteristics. We found that patients living in neighborhoods with the highest deprivation scores (75-100) had the highest odds of post-induction cesarean delivery versus those living in areas experiencing the lowest levels of deprivation (0-24). Importantly, our work expands to risk factors beyond the traditional demographic and clinical factors normally taken into account when considering risk of post-induction cesarean delivery (Grobman, 2012; Levine et al., 2018; Tolcher, 2020).

This study illustrates that there is an association between levels of residential deprivation where one lives, even when adjusting for individual-level covariates. The idea that chronic and acute stress has physical implications for patients is not new, a phenomenon that particularly affects women of color. Therefore, it is plausible that living in a stressful neighborhood, e.g. one with high levels of neighborhood deprivation might impact delivery outcomes. Research by Krieger *et al.*, has demonstrated the effect of neighborhood deprivation on other health outcomes such as cancer (N. Krieger, Feldman, Kim, & Waterman, 2018; Scally, Krieger, & Chen, 2018), assaults (N. Krieger, Feldman, et al., 2017), and excess mortality (Subramanian, Chen, Rehkopf, Waterman, & Krieger, 2005). Work has also been done demonstrating the effect of neighborhood deprivation on pregnancy-related outcomes, such as preterm birth and low birth rate (Vinikoor-Imler et al., 2011). We add to the literature by evaluating the role of neighborhood deprivation in post-induction outcomes. Additionally, the result of our sensitivity analysis assessing the role of residential mobility on adverse post-induction outcomes suggests that mobility during pregnancy amplifies the effect of neighborhood deprivation.

A major strength of our study is our large sample size of inductions (almost 9,000 labor inductions) and our cohort comes from a diverse spectrum of neighborhood deprivation levels with some areas surrounding Philadelphia having very low levels of deprivation and some areas in inner city Philadelphia experiencing very high levels of neighborhood deprivation. This large spread of deprivation levels in terms of our exposure of interest was crucial for our models. In addition, the majority are patients of color. Therefore, in addition to the diversity in terms of neighborhood deprivation exposures, there was also significant racial/ethnic diversity in our cohort. Our diverse cohort was made possible in part due to our utilization of a validated algorithm to identify deliveries within our health system's EHR, ensuring that we captured all patients, allowing for our large cohort size with which to evaluate outcomes of induction.

Importantly, our study assesses the role of neighborhood deprivation on post-induction cesarean delivery as an adverse outcome of induction. We found that patients from more deprived neighborhoods were at greater risk of post-induction cesarean delivery after adjusting for a multitude of confounders already known to increase risk, including race/ethnicity. We included race/ethnicity in our models, understanding that race/ethnicity and its role on post-induction cesarean delivery is not due to biological differences. Rather, in this case, race/ethnicity at the individual-level serves as a proxy for socioeconomic disparities, namely racism (both structural and direct against the individual), and other factors of living as a person of color that are not directly captured in our neighborhood deprivation score. Disparities among post-induction outcomes exist for a multitude of reasons. We explore one such potential mechanism underlying this difference - namely, neighborhood deprivation. Our exposure, neighborhood deprivation, is a representation of a type of structural racism, and explains only part of the racial disparities that exist in healthcare. We retained race/ethnicity in our fully adjusted model to address the racism that individuals may experience at the individual-level, which may differ from the neighborhood-level deprivation that exists due to structural racism.

Limitations of utilizing EHR data include our reliance on coding for billing purposes and therefore our study is subject to misclassification due to coding biases. Additionally, important clinical factors that have been demonstrated to be predictors of cesarean (e.g. cervical exam) were not available to us for the purposes of this study and therefore it is unclear how results may have been changed with inclusion of these parameters. Finally, it would appear that residential mobility amplifies the association between neighborhood deprivation and cesarean delivery after induction; however, we did not have this data for the full cohort, and therefore this analysis exists only for a subset of our cohort as a sensitivity analysis.

In conclusion, this study assesses the role of neighborhood deprivation on labor induction outcomes. In finding that neighborhood deprivation is associated with post-induction cesarean delivery, we are able to illustrate that neighborhood context may be important to the health of those delivering. Given that labor inductions are one of the most commonly performed procedures during pregnancy, and that cesarean deliveries are associated with increased morbidity, it is important that research continues to better identify individual and neighborhood-level risk factors of post-induction cesarean delivery. Importantly, the finding of a clear association with neighborhood deprivation and increased post-induction cesarean risk can inform public health practitioners and policy makers about the importance of evaluating risks among those from less-advantaged neighborhoods and improving neighborhood conditions, respectively.

CHAPTER 5: DISCUSSION

5.1. Conclusions

In this dissertation, we developed a method to aid in the improvement of geo-spatial exposure assignment in longitudinal studies, including those studying pregnancy outcomes, and we investigate individual-level and neighborhood-level risk factors of delivery outcomes, including severe maternal morbidity and post-induction cesarean delivery. In chapter 2, we developed an algorithm titled REMAP to determine whether a patient in a large Electronic Health Record (EHR) has moved or not. This algorithm provides a solution to the problem of exposure misclassification, even in a very large, error-prone EHR, reducing the need for manual review to determine whether a patient has moved. REMAP was 95.7% accurate (95% CI 94.7%-96.7%), outperforming the comparison of ZIP codes alone (82.9% accuracy). In this large urban cohort, 41% of patients moved during pregnancy. Without taking residential mobility during pregnancy into account, we found that 24.4% of patients would be assigned a deprivation score misclassified by at least one quartile. In absolute terms, 39% of patients had a deprivation score that was misclassified at any level. Therefore, taking residential mobility into account is critical to the integrity of longitudinal geo-spatial epidemiology studies. This algorithm is currently shared on GitHub (https://github.com/bolandlab/REMAP) and will be shared later as an R package for others to correctly classify their exposures of study.

In chapter 3, we furthered the research being done on nationally rising rates of SMM, one of the most significant contributors to poor health outcomes for women (Geller et al., 2018). As shown in the literature, we found that certain individual-level characteristics increase one’s likelihood of experiencing an SMM. Namely, being non-White, having a cesarean delivery, a stillbirth, multiple gestation or preeclampsia increase the risk of SMM. Equally as important however, neighborhood-level factors also appear to be important drivers of SMM and suggest that perhaps historic and present-day structural racism and violent crime play a role in rates of SMM. This study’s approach to interrogating both individual- and neighborhood-level covariates is a holistic approach to identifying places for clinical and public health interventions to help explain some of the racial or ethnic differences in the risk of SMM, along with the other known comorbidities of SMM. Importantly, this study highlights, once again, that differences in SMM by race are not biological or due to clinical risk factors alone.

In chapter 4, we take a step in understanding the role that neighborhood deprivation plays in labor induction outcomes. In finding that neighborhood deprivation does indeed increase the risk of cesarean delivery post-induction, we are able to illustrate that neighborhood context is indeed important to the health outcomes of those delivering. Given that labor inductions are one of the most commonly performed procedures during pregnancy, and that cesarean deliveries are associated with increased morbidity, it is important that research is continued to better identify individual and neighborhood-level risk factors of cesarean delivery after induction.

5.2. Limitations

Throughout this work we encountered many limitations, both statistical and epidemiological. In chapter 2, we note that patients' residential histories are compiled from the patient’s encounter with Penn Medicine, when they are asked in the office to confirm their current address. We use the addresses at delivery and closest reported to one year prior to delivery in our analysis. However, there are many obstacles that affect the accuracy of these addresses, including administrative entry errors, some of which we are able to correct for using REMAP. However, there are several reasons, particularly during pregnancy, that the address collected might be a permanent address rather than the address where the patient spends the majority of their time. The patient might use their parent’s address if they live in a residence where the delivery of mail is unreliable. Additionally, the patient might be homeless, living in a homeless shelter, or an otherwise transient living condition, where again they might put down a more permanent address, perhaps a friend’s or parent’s and they may not disclose their living situation due to the stigma associated with being homeless or living in a dwelling that is not one's own. Lastly, a patient might spend the majority of their time at another address, perhaps a significant other's, but use a different mailing address. Thus, there are limitations to the accuracy of these residential histories, and therefore our ability to correctly determine a residential mobility event. By using clinical data in this study, we are limited to the accuracy of the information provided to the medical health provider. The misclassification of these residential mobility events might therefore cause misclassification of the geo-spatial exposure of interest, regardless of use of REMAP. However, we assert that this misclassification would be improved by REMAP, as compared to not accounting for residential mobility at all, which we demonstrate in chapter 2. Qualitative methodologies would have to be employed to further investigate indications for moving and address reporting, which might be missed in our study. These qualitative methods may be especially helpful in the issue of a failure to report moving is due to some stigma, either perceived or actualized on the part of the patient in reporting to the information to clinicians. Also, those who have insufficient means to pay for their healthcare (for a variety of means) may be less inclined to report an accurate address to the hospital as it is well known that the address on record is where the bills will be send.

In chapter 3, we note that our study faces certain limitations despite its multiple strengths. First, we used the composite outcome of severe maternal morbidity, which although an established CDC measure of maternal morbidity, it obscures the nuance of maternal morbidity. Namely, while we can make clinical recommendations based on this broad outcome, some clinicians would argue that it would be more useful to design interventions for those particular conditions that drive the trend of increasing severe maternal morbidity. However, by studying this outcome we are able to contribute to severe maternal morbidity research and compare Penn Medicine data with nationally reported data through the CDC. Additionally, there are always limitations that come from utilizing EHR data, as it is reliant on coding for billing purposes and is therefore subject to misclassification and lack of availability of all covariates of interest. For example, we were unable to include variables such as parity in our full models as data were not available specifically for that covariate for a large enough cohort. Additionally, our study spans 2010-2017, during which time billing codes transitioned from ICD-9 to ICD-10. Diagnosis and procedural codes became more granular with the introduction of ICD-10 codes in 2015 and therefore possible misclassification for variables, such as blood transfusions, could occur.

In chapter 4, we encountered limitations as well. Per the aforementioned limitations of working with EHR data, not all variables of interest were available to us for our full cohort of inductions. For example, we were unable to include variables such as residential mobility and cervical exam information in our full model as data were not available specifically for those covariates. In the case of cervical exam, we didn't have this data for any patients. However, we were able to conduct a sensitivity analysis with residential mobility, which does add strength to our analysis. This study focuses on mostly "low-risk" patients receiving labor inductions in the University of Pennsylvania Health System. We excluded patients who had a prior-cesarean, had a stillbirth, multiple gestation, and a premature delivery (earlier than 37 weeks). While this is not a limitation of the study directly, it is a limitation of the study's generalizability at-large. It is important for the purpose of research translation that it is clear that the conclusions drawn from these data are inherently specific to this "low-risk" population and cannot be generalized to all people for whom an induction is clinically indicated.

5.3. Future directions

In this dissertation we contribute research with the potential to impact the rising trends in maternal morbidity and mortality seen in the United States. Specifically, in chapter 2 we presented REMAP to be incorporated into the methodological toolkit of reproductive and maternal and child health researchers, and in chapters 3 and 4 we sought to better characterize the risk factors of severe maternal morbidity and post-induction cesarean delivery. In chapter 2, we developed REMAP, and also through our study population characterized residential mobility in a Penn Medicine cohort of pregnant patients. In this study however, we were not able to answer the question of why pregnant people in this population moved, and importantly why some moved to neighborhoods of lower or greater levels of neighborhood deprivation. Therefore, in the future we would be interested in understanding qualitatively, who moves, and the associated upward or downward mobility in terms of neighborhood deprivation. We would hope to use qualitative methods to conduct semi-structured interviews with Penn Medicine patients, so as to better answer this question. Additionally, in the future we would like to look at the association between residential mobility itself and severe maternal morbidity and cesarean delivery after induction. While we conducted a sensitivity analysis with residential mobility in chapter 4, we did not have that information for the full-cohort.

In building from chapter 3, we would like to consider other comorbidities such as uterine myomata, which is at increased rates among older delivering patients of color, to assess what affect this may have on incidence of severe maternal morbidity in our population along with neighborhood-level effects. Further, we noted the limitations of using a composite outcome such as severe maternal morbidity. In future studies, we would like to parse apart severe maternal morbidity so as to better understand which indicators are truly driving the increased rates of severe maternal morbidity, perhaps through the use of machine learning techniques. Additionally, it would be interesting to see if the associations we found for severe maternal morbidity as a whole, would hold with some of the more ubiquitous indicators, such as hemorrhaging. By pulling the composite outcome into its more discrete pieces, we would be able to offer clinicians more concrete recommendations about places for intervention. For example, if hemorrhaging is the most important indicator, perhaps Penn Medicine would want to consider implementing hemorrhaging “crash carts” on their labor and delivery floors, as other hospital systems have. Lastly, we would be interested in taking a more direct look at the role of racism in severe maternal morbidity, modelling off some of Nancy Krieger’s work with racism, including utilizing historic redlining and segregation indices.

In chapter 4, we conducted our study of cesarean versus vaginal deliveries among a relatively "low-risk" population of patients who undergo labor induction. In the future, it would be of use to conduct a similar study among a more "high-risk" population, so as to offer insights into the association between neighborhood deprivation and cesarean delivery after induction among this population as well. Indeed, a labor induction is often indicated for patients in this "high-risk" category. Further, we would like to look at spontaneous vaginal birth as well. Success of induction for delivering patients is often seen as a vaginal delivery but this category could further be parsed out into spontaneous vaginal birth, which is often what patients and clinicians hope for during a delivery, a vaginal delivery that does not necessitate use of forceps or vacuum extraction. Lastly, we think that it would be interesting to access the role of genetics on these outcomes to better understand the effect of the genetic-environment interaction on labor induction outcomes.

5.4. Clinical Implications

In chapter 2, we displayed that residential mobility is important to consider when studying geo-spatial exposures so as to avoid exposure misclassification. This is critical for the formation of unbiased clinical recommendations. Furthermore, we demonstrated that in our urban cohort of pregnant patients, the rate of residential mobility within a year of pregnancy is high, around 41%. This might be important for clinicians to note and take into consideration when creating care plans for their patients. In chapter 3, we illustrate that neighborhood-level race and violent crime were associated with increased levels of severe maternal morbidity. Clinicians may want to consider screening patients for neighborhood-level crime for risk-based severe maternal morbidity screening; however, it is critical that clinicians not perpetuate racial biases that are not biological. Clinicians should be aware that the differences in race and severe maternal morbidity that we found are likely due to the social construction of race and the structural racism persistent in the United States. In chapter 4 we demonstrate that living in more deprived neighborhoods increases a patient's odds of having a post-induction cesarean delivery. What we illustrate through this finding is the impact that living in a stressful neighborhood has on delivery outcomes among pregnant patients. Neighborhood deprivation is a proxy for one type of structural racism, and can only explain a part of the experience that patients of color experience in the healthcare system. Effort needs to be made to design clinical and public health interventions that seek to combat racism and lower rates of severe maternal morbidity and maternal mortality and post-induction cesarean delivery, among other adverse delivery outcomes.

Through this dissertation, and in future work, we hope to contribute to the body of literature supporting women's health. Rising rates of maternal morbidity and mortality in the United States has continued for too long, affecting and claiming the lives of many women. It is with this in mind that we hope to continue in this work, with the idea that these studies and others have the potential to make a real difference in clinical outcomes for delivering people.

APPENDIX A: CHAPTER 2 DETAILS

Address 1-year Prior to Delivery	Address at Delivery
1 Cherry Tree **St**, Apt Z104 Swedesboro NJ 08085	1 Cherry Tree **Street**, Apt Z104 Swedesboro NJ 08085

No Move
Difference between St vs. Street ignored

1 Cherry Tree Dr, Apt **#104** Swedesboro NJ 08085	1 Cherry Tree Drive, Apt **Z104** Swedesboro NJ 08085

No Move
Difference between Apartment # ignored

1 **Cherr** Dr, Apt #104 Swedesboro NJ 08085	1 **Cherry Tree** Drive, Apt Z104 Swedesboro NJ 08085

No Move
Less then or equal to 5 Character Differences Ignored

1 Cherry Tree Dr, Apt Z104 **Swedesboro** NJ 08085	**1** Cherry Tree Drive, Apt Z104 **Woolwich Township** NJ 08085

No Move
Address # (1) is the same and no Character Differences in Street line – Township Ignored

1 Cherry Tree Dr, Apt Z104 Swedesboro NJ 08085	**2** Cherry Tree Drive, Apt Z104 Swedesboro NJ 08085

Move
Address # (1 vs. 2) is Different

Figure A.1: Examples of algorithm decision making with a sample address.

APPENDIX B: CHAPTER 3 DETAILS

Table B.1: ICD-9 and ICD-10 codes for preeclampsia and diabetes variables

CODE	CODE STANDARD NAME	CODE DESCRIPTION
		Preeclampsia and eclampsia and other types of hypertension
642.0x	ICD-9-CM	Benign essential hypertension complicating pregnancy, childbirth, and the puerperium
642.1x	ICD-9-CM	Hypertension secondary to renal disease, complicating pregnancy, childbirth, and the puerperium
642.2x	ICD-9-CM	Other pre-existing hypertension complicating pregnancy, childbirth, and the puerperium
642.3x	ICD-9-CM	Transient hypertension of pregnancy
642.9x	ICD-9-CM	Unspecified hypertension complicating pregnancy, childbirth, and the puerperium
642.4x	ICD-9-CM	Mild or unspecified pre-eclampsia
642.5x	ICD-9-CM	Severe pre-eclampsia
642.6x	ICD-9-CM	Eclampsia
642.7x	ICD-9-CM	Pre-eclampsia or eclampsia superimposed on pre-existing hypertension
O14x	ICD-10-CM	Preeclampsia ranging from mild to severe and unspecified
O15x	ICD-10-CM	Eclampsia
O11x	ICD-10-CM	Preexisting Hypertension with Preeclampsia
		Diabetes
648x	ICD-9-CM	Diabetes complicating pregnancy
250x	ICD-9-CM	Diabetes mellitus types I and II ranging from controlled to uncontrolled
O24x	ICD-10-CM	Diabetes in pregnancy, childbirth, and the puerperium

Table B.2: Sources and data files for neighborhood-level covariates included in our spatial regression model		
Neighborhood-Level Covariate	**Source**	**Data File**
Prop. of women aged 15-50 years in each census tract below 100 percent poverty level	ACS	S1301
Prop. of women aged 15-50 years in each census tract that graduated high school (including equivalency)	ACS	S1301
Prop. of women aged 16-50 years in each census tract that are in the labor force	ACS	S1301
Prop. of women aged 15-50 years in each census tract that received public assistance income in the past 12 months	ACS	S1301
Prop. of occupied housing units in each census tract that are owner-occupied	ACS	S2502
Prop. of occupied housing units in each census tract that are renter-occupied	ACS	S2502
Median family income (dollars)	ACS	S1903
Prop. of each census tract that identifies as Asian Alone	ACS	B01001D
Prop. of each census tract that identifies as Black or African-American	ACS	B01001B
Prop. of each census tract that identifies as Hispanic or Latinx	ACS	B01001I
Prop. of each census tract that identifies as White Alone	ACS	B01001A
Housing Violations	OpenDataPhilly	
Violent Crime Rate	OpenDataPhilly	
Non-Violent Crime Rate	OpenDataPhilly	

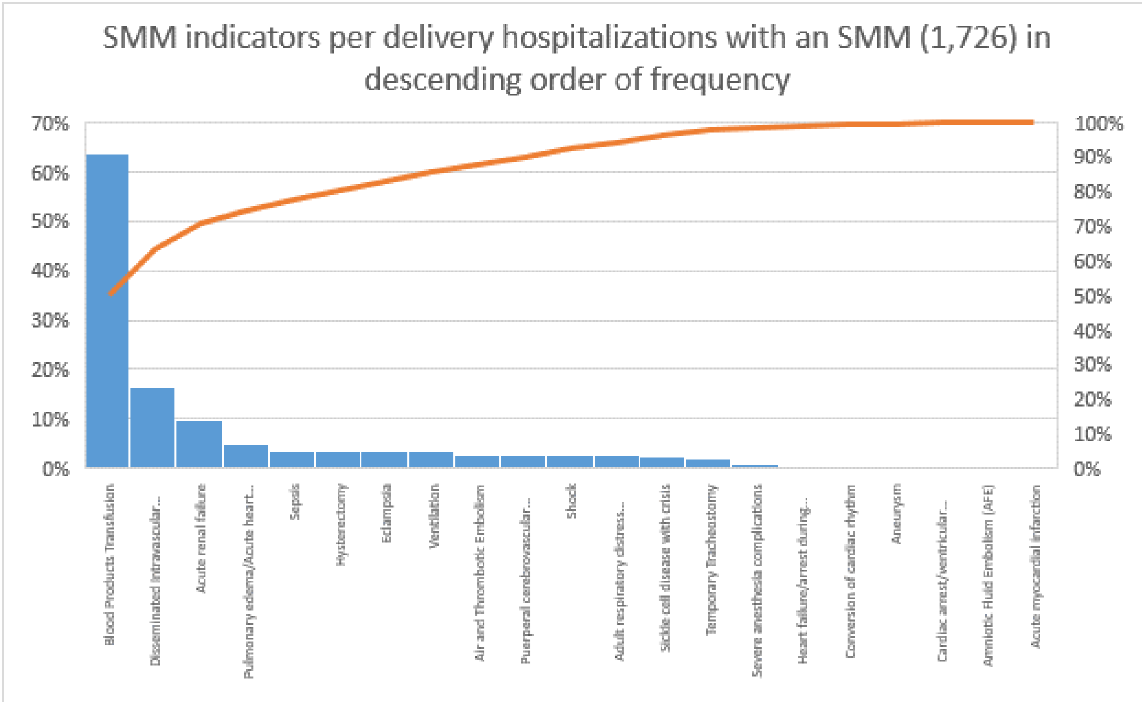

Figure B.1: The distribution of the 21 SMM indicators per 63,334 hospital deliveries in the University of Pennsylvania Hospital System in a descending order of frequency, with a cumulative line on a secondary axis as a percentage of the total.

Table B.3: Individual risk factors for severe maternal morbidity - univariable and multivariable analysis (sensitivity analysis for unique patients only)				
Risk Factor	**OR**	**95% CI**	**aOR**	**95% CI**
Race/Ethnicity				
Hispanic	0.95	0.77-1.15		
Non-Hispanic				
Black or African American	1.26	1.13-1.40	1.02	0.86-1.2
White	0.69	0.61-0.77	0.73	0.61-0.88
Asian	1.34	1.09-1.62	1.4	1.09-1.77
American Indian or Alaskan Native	1.58	0.39-4.24		
Hawaiian or Pacific Islander	0.87	0.14-2.75		
Other	1.07	0.84-1.34		
Age	1.01	1.00-1.01		
Weight	1.00	1.00-1.00		
Height	1.00	0.97-1.03		
BMI	1.00	0.99-1.00		
Cesarean delivery	3.66	3.28-4.09	3.4	3.02-3.80
Stillbirth	3.52	2.47-4.87	4.35	3.02-6.09
Multiple gestation	2.25	1.76-2.84		
Preterm birth	2.08	1.76-2.44	1.53	1.28-1.80
Diabetes	1.45	1.15-1.81		
Preeclampsia	3.69	3.27-4.16	2.86	2.53-3.24

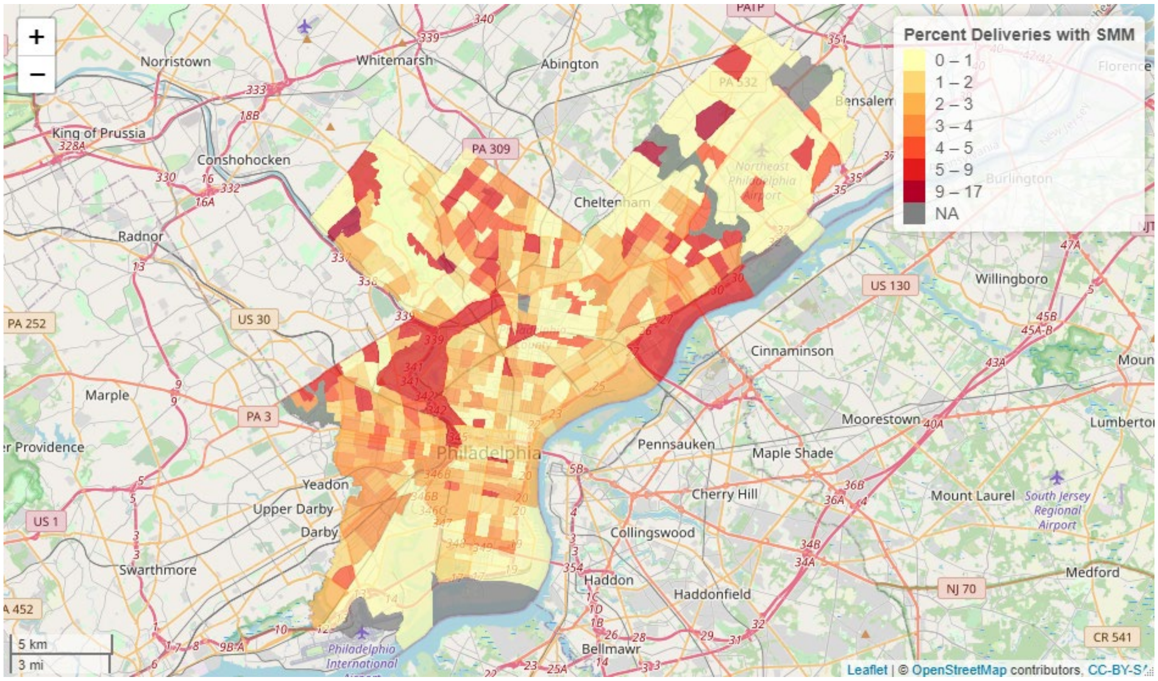

Figure B.2: The Percent of deliveries with SMM out of the total deliveries per each census tract.

Table B.4: Results of univariable spatial regression analysis of neighborhood-level covariates on percent of deliveries with a severe maternal morbidity (SMM) per census tract

Neighborhood-Level Covariate	Estimate	% Change in SMM Rate*	P-value
Percent of each census tract that identifies as **Black or African-American** Alone	0.001	0.15	<0.001
Percent of each census tract that identifies as **White** Alone	-0.002	-0.15	<0.001
Number of Violent Crimes (log-transformed variable)	0.049	4.90	<0.001
Percent of occupied housing units in each census tract that are **renter-occupied**	0.000	0.05	<0.001
Housing Violations (log-transformed variable)	0.039	3.90	0.002
Percent of women aged 15-50 years in each census tract that **graduated high school** (including equivalency)	0.003	0.29	0.003
Median family **income** (dollars) (log-transformed variable)	-0.062	-6.20	0.011
Percent of each census tract that identifies as **Asian** Alone	-0.003	-0.33	0.03
Percent of women aged 15-50 years in each census tract that **received public assistance** income in the past 12 months	0.004	0.40	0.043
Percent of women aged 15-50 years in each census tract below 100 percent **poverty** level	0.001	0.11	0.128
Percent of each census tract that identifies as **Hispanic or Latinx**	-0.001	-0.08	0.222
Non-Violent Crime Rate (log-transformed variable)	0.020	2.00	0.305
Percent of occupied housing units in each census tract that are **owner-occupied**	-0.001	-0.05	0.467
Percent of women aged 16-50 years in each census tract that are **in the labor force**	-0.001	-0.05	0.618

*Percent change in the rate of SMM per a one unit-increase in neighborhood-level covariate

Table B.5: results of multivariable spatial regression analysis of neighborhood-level covariates on percent of deliveries with a severe maternal morbidity (SMM) per census tract			
Neighborhood-Level Covariate	**Estimate**	**% Change in SMM Rate***	**P-value**
Prop. of each census tract that identifies as **Black or African-American** Alone	0.002	0.24	0.020
Number of Violent Crimes (log-transformed variable)	0.030	3.0	0.061
Prop. of each census tract that identifies as **White** Alone	0.001	0.15	0.215
*Percent change in the rate of SMM per a one unit-increase in neighborhood-level covariate			

APPENDIX C: CHAPTER 4 DETAILS

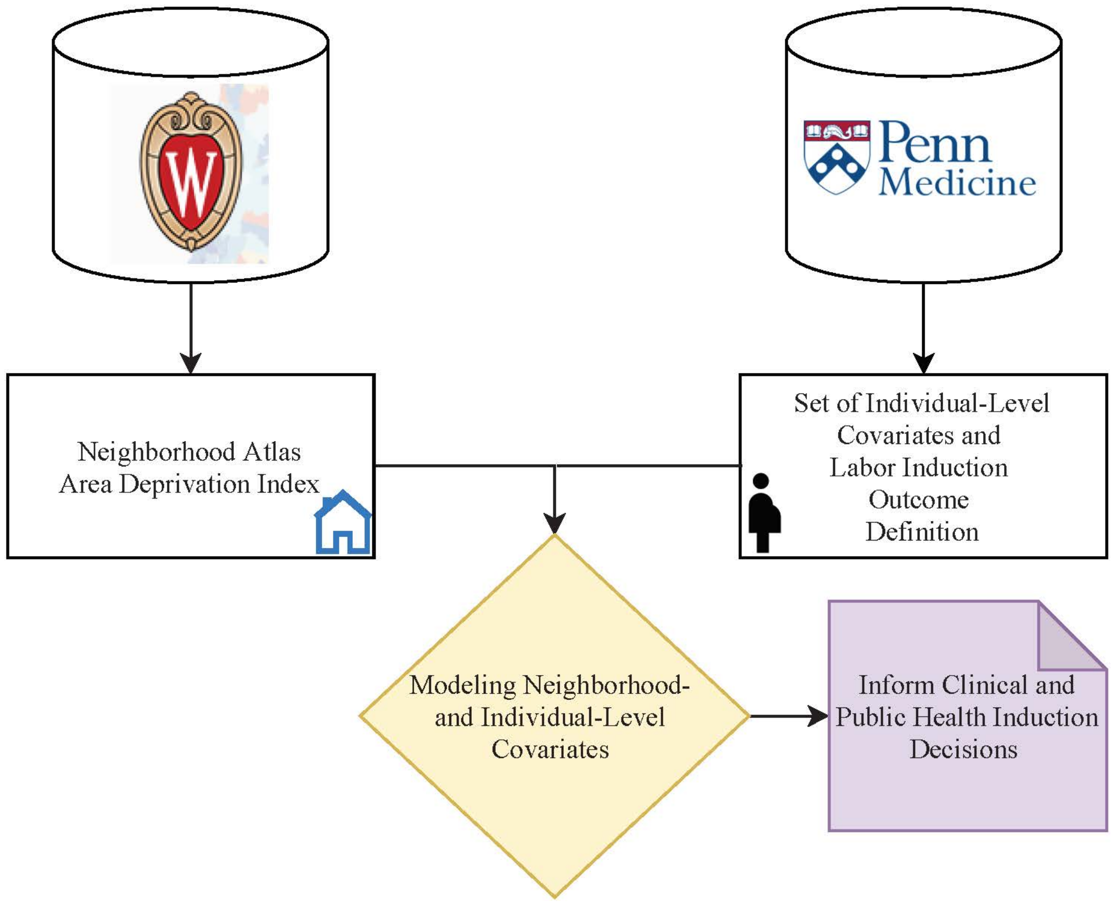

Figure C.1: Overview of our methodology to model individual-level covariates from the Penn Medicine EHR and neighborhood-level covariates from public sources on labor induction outcomes, so as to better inform clinical and public health decisions.

Table C.1: ICD-9 and ICD-10 codes used to identify labor induction from the EHR		
CODE	**ICD-9 or ICD-10**	**DESCRIPTION**
73.01	ICD-9	Induction of labor by artificial rupture of membranes
73.1	ICD-9	Surgical induction of labor
73.4	ICD-9	Medical induction of labor
10907ZC	ICD-10	Artificial rupture of membranes (not in augmentation)
0U7C7DZ	ICD-10	Dilation of cervix with intraluminal device, via natural or artificial opening (Foley balloon left in on discharge)
0U7C7ZZ	ICD-10	Dilation of Cervix, via natural or artificial opening (Foley balloon)
3E0P7GC	ICD-10	Cervical ripener (cervidil, misoprostol etc...)
3E033VJ	ICD-10	Oxytocin or Pitocin not used for hemorrhage or labor augmentation

Table C.2: Sensitivity analysis for associations between neighborhood deprivation and cesarean delivery following labor induction + residential mobility

Covariate	Crude OR	95% CI	Adjusted OR a	95% CI
Neighborhood Deprivation				
Highest (75-100)	0.90	0.78-1.03	2.12	1.51-2.96
High (50-74)	1.07	0.91-1.26	2.24	1.59-3.15
Moderate (25-49)	0.91	0.77-1.06	1.20	0.87-1.67
Lowest (0-24)	1.00	Reference	1.00	Reference
Comorbidities				
Diabetes (versus no diabetes)	1.30	1.03-1.58	0.94	0.65-1.37
Pregnancy-related hypertension (versus not)	1.59	1.41-1.80	1.24	0.98-1.57
Obesity (versus not obese)	1.76	1.58-1.97	2.14	1.75-2.60
Residential Mobility (moved versus no)	1.13	0.96-1.33	1.12	0.93-1.33

aAdditionally adjusted for maternal age (continuous), race/ethnicity, parity, gestational age, and marital status

Table C.3: Adjusted* odds ratios and their 95% confidence intervals for various regression models of the association between neighborhood deprivation and post-induction cesarean delivery

Model	Level of Neighborhood Deprivation	aOR	95% CI
Model 1: generalized linear mixed model, categorical neighborhood deprivation levels and post-induction cesarean delivery	Highest	1.29	1.05-1.57
	High	1.28	1.04-1.57
	Moderate	1.20	1.00-1.44
	Lowest	1.00	Reference
Model 2: genearlized linear mixed model, association between neighborhood deprivation as a non-linear spline and post-induction cesarean delivery	Highest	1.21	1.10-1.34
	High	1.14	1.11-1.18
	Moderate	1.07	1.04-1.10
	Lowest	1.00	Reference
Model 3: Model 1 + residential mobility on a subset for whom we had residential mobility data	Highest	2.12	1.51-2.96
	High	2.24	1.59-3.15
	Moderate	1.20	0.87-1.67
	Lowest	1.00	Reference

*adjusted for obesity, pregnancy-related hypertension, diabetes, parity, gestational age, patient age, marital status, race/ethnicity

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